THE Journal Kansas Medical Society

SEPTEMBER
1961

VOL LXII
NO IX

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(1) Carter, S.: *M. Clin. North America* 37:315, 1953.
(2) Maltby, G. L.: *J. Maine M. A.* 48:257, 1957.
(3) Buchthal, F.; Svensmark, O., & Schiller, P. J.: *Arch. Neurol.* 2:624, 1960.

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Volume LXII, Number 9—September, 1961

The JOURNAL of the KANSAS MEDICAL SOCIETY

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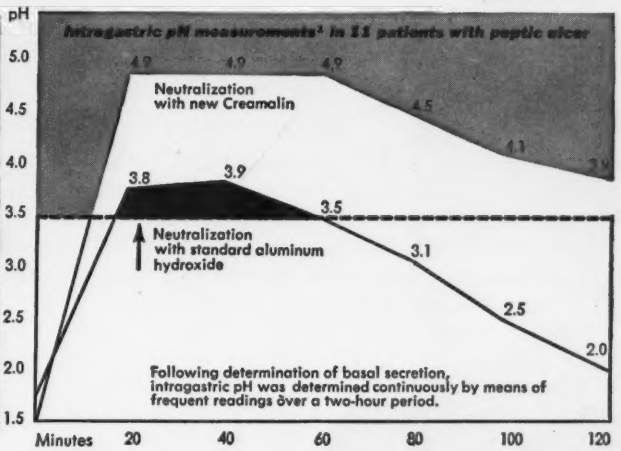

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Bibliography *(13 clinical studies, 858 patients)*: **1.** Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. **4.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **5.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **6.** Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. **7.** Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. **8.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression – New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **9.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **10.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **11.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **12.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. **13.** Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

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3. Fernandez-Herlihy, L: Lahey Clinic Bull. 11:12 (July-Sept.) 1958.

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infectious diseases Infections cause a lowering of ascorbic acid levels in the plasma; and the absorption of this vitamin is reduced in diarrheal states.[7] 7. Goldsmith, G A.: Conference on Vitamin C. The New York Academy of Sciences, New York City, Oct. 7 and 8, 1960. Reported in: Medical Science 8:772 (Dec.10) 1960.

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8. Duncan G. G.: Diseases of Metabolism 4th edition W. B. Saunders, Philadelphia, 1959, p. 812. 9. Pollack, H.: Am. J. Med. 25:708 (Nov.) 1958.

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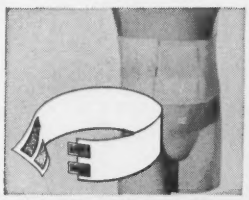

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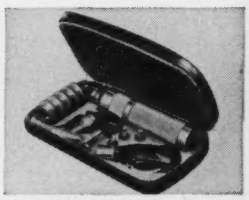

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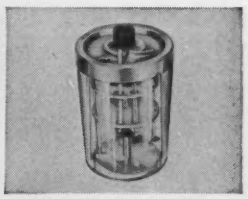

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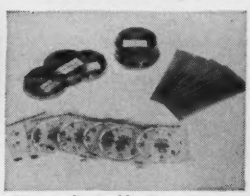

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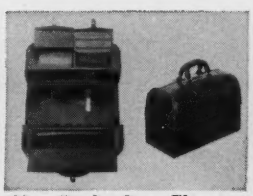

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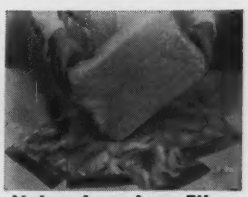

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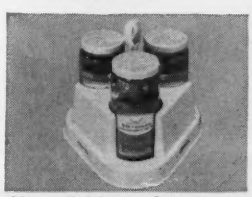

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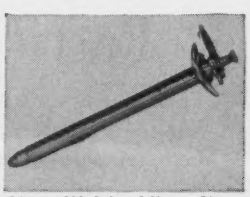

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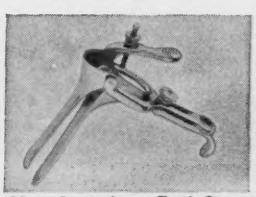

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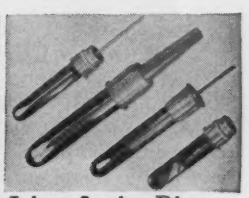

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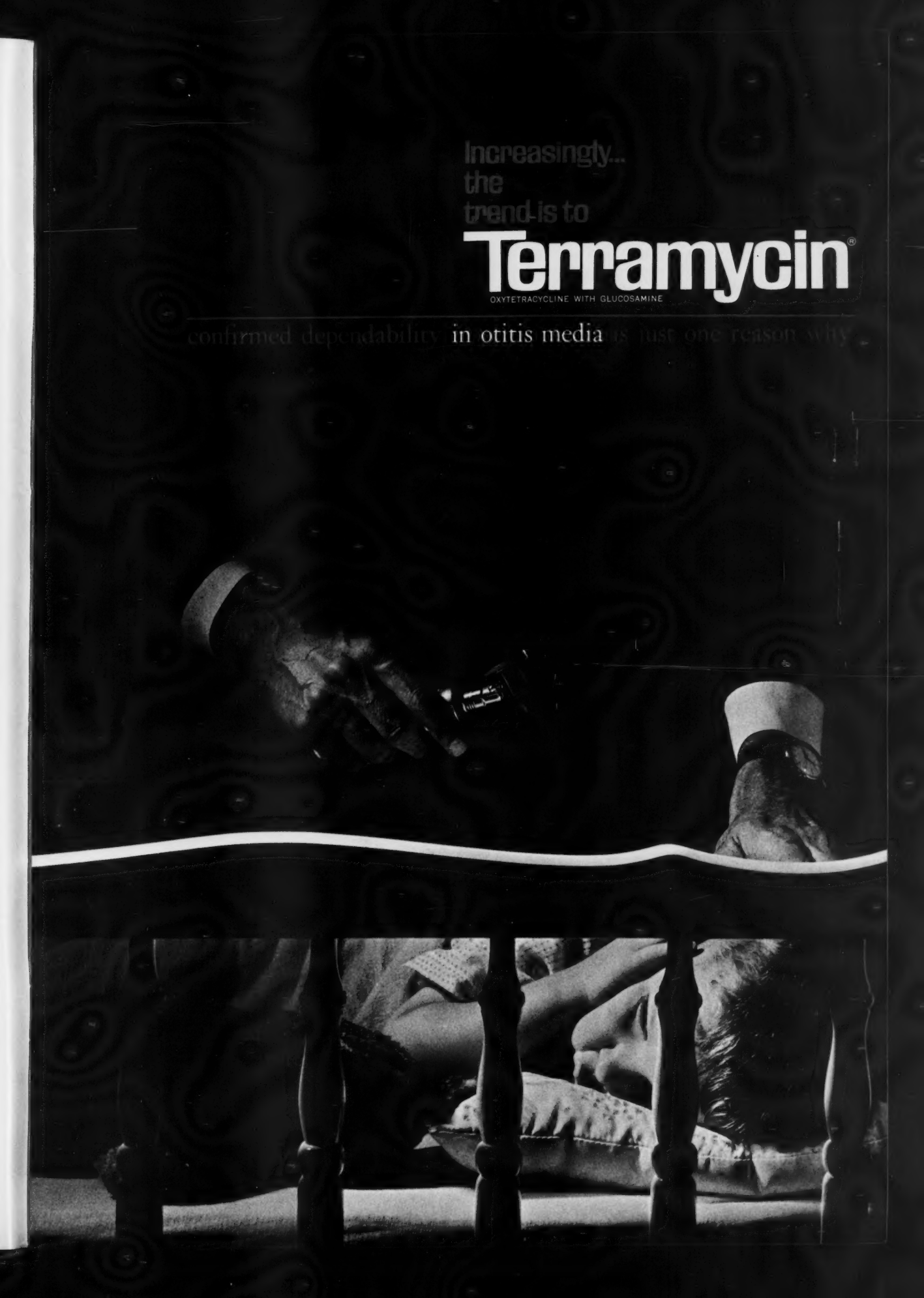
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*Jacques, A. A., and Fuchs, V. H.: J. Louisiana M. Soc. 113:200, May, 1961.

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Accordingly, and effective immediately, forms incorporating glucosamine will be offered simply as Terramycin without the "Cosa" prefix.

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We feel certain that this action, prompted by your comments and those of many other physicians, will simplify your writing of prescriptions for Terramycin products.

We welcome your comments on this action and on any other phase of our operations, since it is our objective to render every service as efficiently as possible to our friends in the medical profession.

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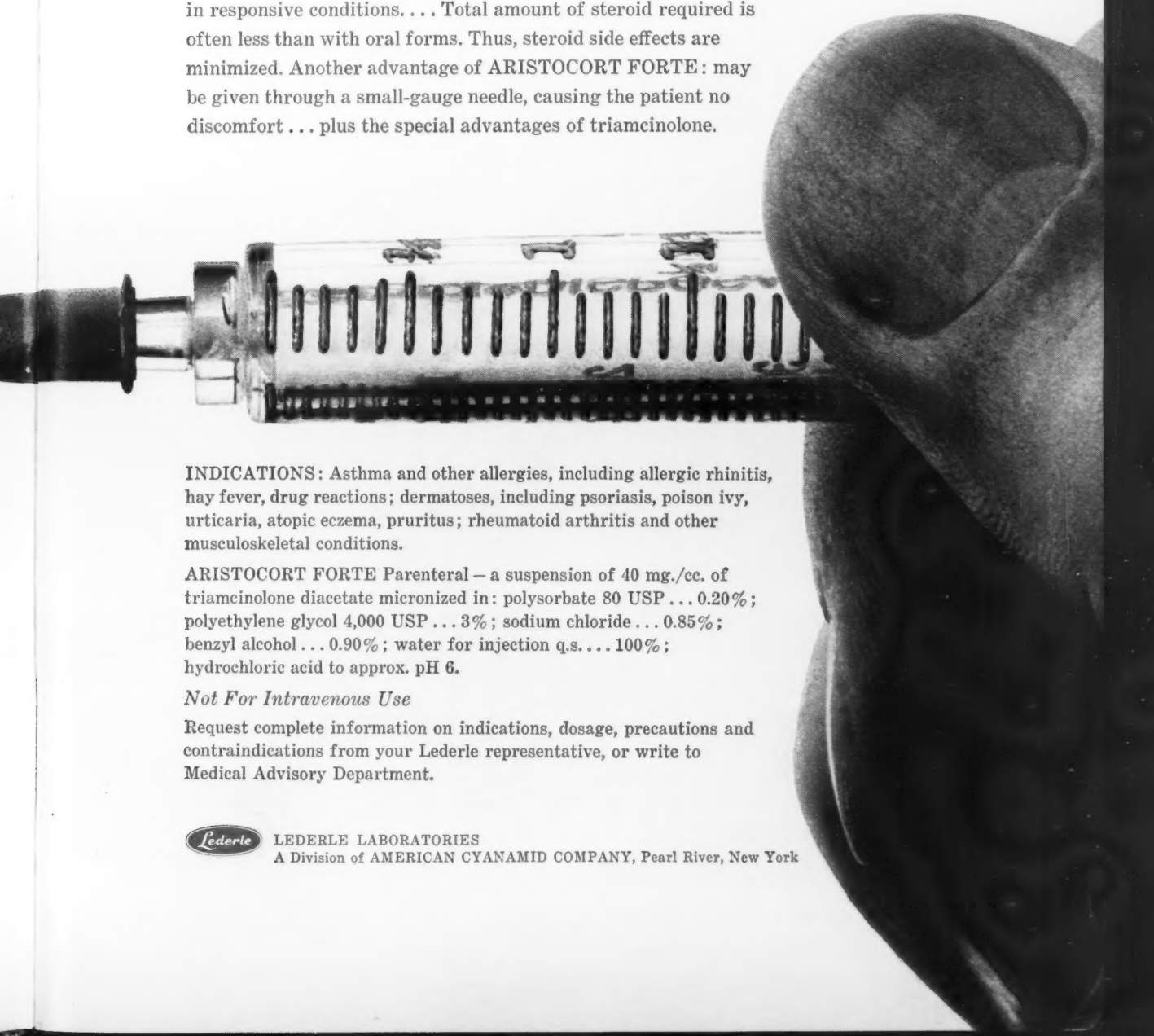

INDICATIONS: Asthma and other allergies, including allergic rhinitis, hay fever, drug reactions; dermatoses, including psoriasis, poison ivy, urticaria, atopic eczema, pruritus; rheumatoid arthritis and other musculoskeletal conditions.

ARISTOCORT FORTE Parenteral—a suspension of 40 mg./cc. of triamcinolone diacetate micronized in: polysorbate 80 USP . . . 0.20%; polyethylene glycol 4,000 USP . . . 3%; sodium chloride . . . 0.85%; benzyl alcohol . . . 0.90%; water for injection q.s. . . . 100%; hydrochloric acid to approx. pH 6.

Not For Intravenous Use

Request complete information on indications, dosage, precautions and contraindications from your Lederle representative, or write to Medical Advisory Department.

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A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

WHENEVER COUGH THERAPY IS INDICATED

HYCOMINE®

Syrup

THE COMPLETE Rx FOR COUGH CONTROL

cough sedative | antihistamine
nasal decongestant | expectorant

▪ relieves cough and associated symptoms in 15-20 minutes ▪ effective for 6 hours or longer ▪ promotes expectoration ▪ rarely constipates ▪ agreeably cherry-flavored

Each teaspoonful (5 cc.) of HYCOMINE® Syrup contains:

Hycodan®		
Dihydrocodeinone Bitartrate (Warning: May be habit-forming)	5 mg.	6.5 mg.
Homatropine Methylbromide	1.5 mg.	
Pyrilamine Maleate		12.5 mg.
Phenylephrine Hydrochloride		10 mg.
Ammonium Chloride		60 mg.
Sodium Citrate		85 mg.

Average adult dose: One teaspoonful after meals and at bedtime. May be habit-forming. Federal law permits oral prescription.

Literature on request

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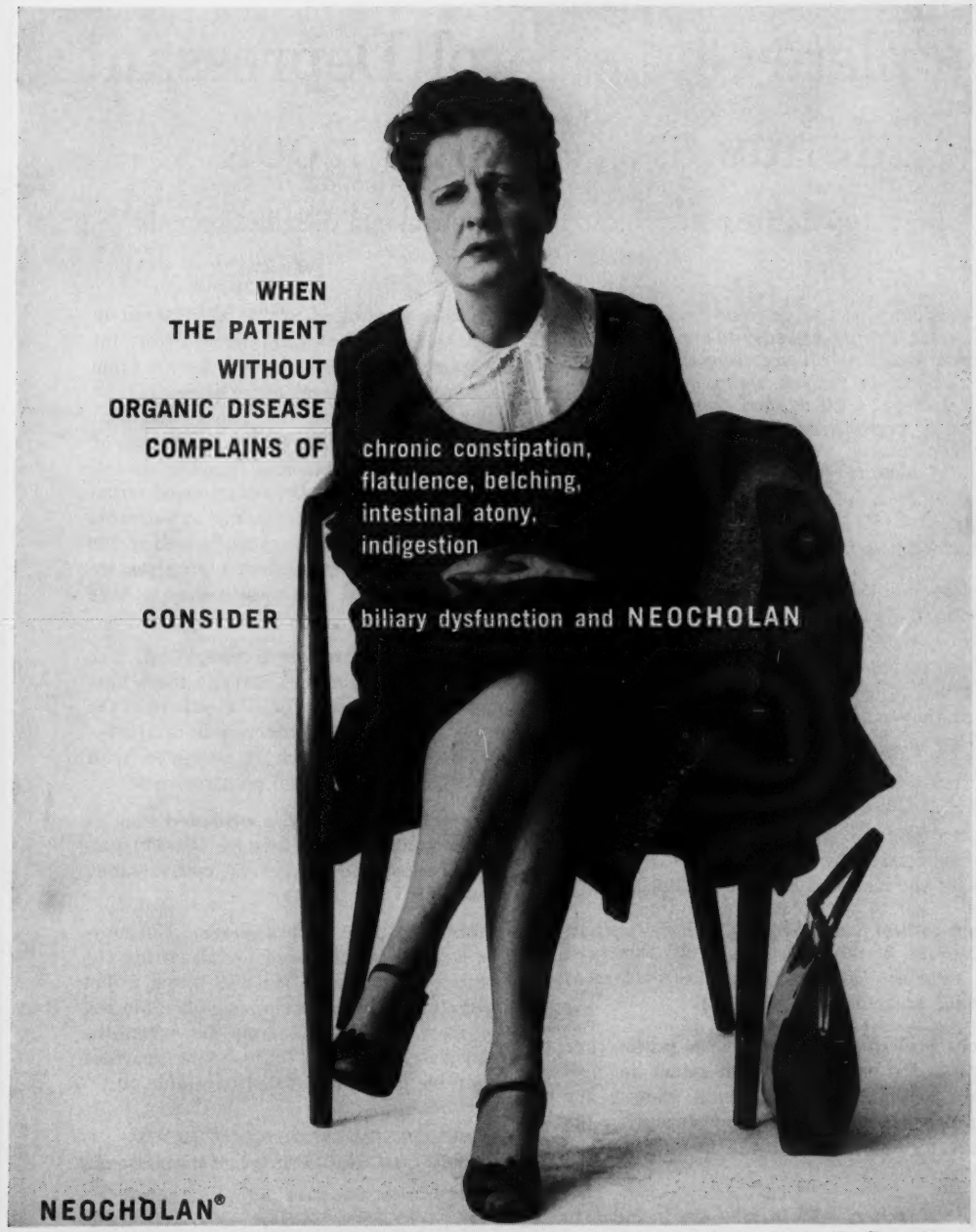
Richmond Hill 18, New York

*U.S. Pat. 2,630,400



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Each tablet provides: Dehydrocholic Acid Compound, P-M Co. 265 mg. (Dehydrocholic Acid, 250 mg.); Homatropine methylbromide 1.2 mg.; Phenobarbital 8.0 mg. Supplied in bottles of 100 tablets.

PM

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Available only to physicians for their distribution—

Complete Cholesterol Depressant Menus and Recipe Book

A new, authoritative patient-aid . . . for professional distribution only

Now available for use in your practice from The Wesson People . . . easy-to-use manual of 40 pages, including all necessary diet instructions . . . menus, recipes, shopping and cooking guidance . . . all worked out for you . . . so arranged and printed that you have only to check the desired daily calorie level before giving the book to your patient.

You will find this book invaluable for treating patients with elevated serum cholesterol.

Complete menus for 10 days enable you to prescribe diets which are appetizing, nutritiously adequate and which can exert cholesterol depressant activity. Special attention has been given to constructing the menu patterns so that they adhere as closely as permissible to the patient's normal eating habits.

NRC Standards fulfilled. Each menu has been calculated to provide the proper daily allowance of proteins, vitamins and other nutrients as recommended by the Food and Nutrition Board of the National Research Council.

Weight control is achieved as each day's menu is given at 3 calorie levels—1200, 1800 and 2600 calories. You prescribe the level most desirable and modify as desired.

Variety and appetite appeal for patient are built into the menu plan to an extent not previously accomplished. Alternate choices for main dishes minimize monotony, encourage the patient to follow closely the menu plan you specify.

Complete recipes—65 in all—are included to assure that the specified menus provide prescribed levels of calories, the pre-determined ratio of poly-unsaturated to saturated fat, plus essential nutrients.

Dietary fat is controlled so that approximately 36% of the total calories are derived from fat and at least 40% of these fat calories are from poly-unsaturated components (linoleates) as found in pure vegetable oil. The replacement of saturated dietary fat by this percentage of poly-unsaturated fat has been found in clinical studies most effective in the reduction of serum cholesterol and in its maintenance at desirable levels. More liberal menus are provided for maintenance after the patient's progress indicates that desired therapeutic results have been accomplished.

Family meal preparation is simplified. The menus are planned around favorite foods having wide appetite appeal for all members of the household. Patients can entertain in comfort—enjoy cakes, cookies, snacks, prepared with recipes which meet medical requirements.

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Adaptable for use with diabetics. Carbohydrates have been calculated to fall within the acceptable range for patients to whom a diet planned for diabetes is important. Calories, which must be supplied from fat when the carbohydrate intake is limited, are provided by desirable poly-unsaturated vegetable oil.

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Wesson is 100% cottonseed oil—winterized and of selected quality

Linoleic acid glycerides (poly-unsaturated)	50-55%
Oleic acid glycerides (mono-unsaturated)	16-20%
Palmitic, stearic and myristic glycerides (saturated)	25-30%
Phytosterol (Predominantly beta sitosterol)	0.3-0.5%
Total tocopherols	0.09-0.12%

Never hydrogenated—completely salt free

Poly-unsaturated Wesson is unsurpassed by any readily available brand, where a vegetable (salad) oil is medically recommended for a cholesterol depressant regimen.

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Please send_____free copies of
"Your Cholesterol Depressant Diet Cook Book" for use with patients.

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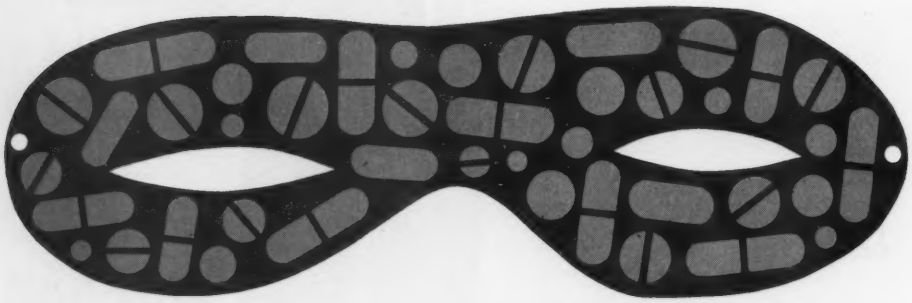
CITY_____ ZONE_____ STATE_____



drugs anonymous

One of the several hastily conceived and potentially dangerous suggestions for reducing drug costs is generic-name prescribing. The proponents of generic-name prescribing claim that it will lower drug costs significantly and—through supervision by the Federal Government—provide quality equivalent to that of trademarked drugs. We maintain that these claims are false. Here are some authoritative answers to the principal questions posed by generic-name prescribing.

How much money would be saved if all prescriptions were written for generic-name drugs?

"The [Rhode Island] Division of Public Assistance examined 10,000 drug prescriptions for welfare recipients for the purpose of determining the actual savings . . . of generic versus trade-name drugs. The drugs had cost $28,000. Substituting generic drugs whenever possible would have provided a saving of less than 5 per cent. Syracuse has made a similar study of drug costs with comparable results."

Rhode Island Medical Journal,
January, 1961

Are the savings worth the risk of sacrificing quality?

". . . it is unsafe [to prescribe generically] because there is not sufficient policing of our standards. . . ."

Lloyd C. Miller, Ph. D.
Director of Revision of the U.S.P.

"The naive belief that, if a product was not good, the FDA would prohibit its sale is just not realistic. . . . it is completely impossible for the FDA to check every batch of every product of every manufacturer. . . . Hence the integrity and reputation of the manufacturer assume unusual significance where drugs and health products are concerned."

Albert H. Holland, M.D.
formerly Medical Director of the
Food and Drug Administration

Smith Kline & French Laboratories, Philadelphia

Schering

Perhaps you have hesitated to prescribe the benefits of a topical steroid because of concern about effectiveness or high cost.

Perhaps you have felt that the usual packaging of topical steroids provides inadequate, uneconomical quantities to suffice for a complete course of treatment.

If any of these considerations reflects your thinking, we believe you will be interested to learn that a truly effective and reasonably priced topical steroid now is available for your patients with dermatologic disorders... DILODERM™ Cream (brand of dichlorisone acetate).

As to effectiveness, here is what a recent report* stated on the use of DILODERM in 53 cases of poison ivy dermatitis: "A satisfactory response...was seen in all cases. There were no cases of primary irritation or other side effects...."

As a matter of fact...you will find not only that DILODERM Cream is exceptionally beneficial in a wide variety of dermatoses responsive to topical steroids, but also that it costs *less* in most instances than generic hydrocortisone creams. In addition, DILODERM affords even greater savings over other topical steroids. Actually, the 15 Gm. tube of DILODERM Cream costs less than virtually all all other topical steroid preparations now prescribed.

As a matter of economy...the 15 Gm. tube of DILODERM is ideally suited for the treatment of large skin areas or extensive lesions. It *covers more* with *less waste;* it provides three times as much medication for only slightly more than double the cost of a small 5 Gm. tube of unbranded hydrocortisone.

We believe your patients with dermatoses will appreciate the significant savings DILODERM Cream affords, and that you, too, will agree... DILODERM in the 15 Gm. tube is *effective, economical in price,* and *even more economical in use.*

Also available: DILODERM Cream, 5 Gm. tube; NEO-DILODERM® Cream 0.25%, 5 and 15 Gm. tubes; DILODERM and NEO-DILODERM Foam, 10 Gm. dispensers; DILODERM and NEO-DILODERM Aerosols, 50 Gm. containers.

*Gant, J. Q., Jr.: *M. Ann. District of Columbia 30*:267, 1961.

If concern about effectiveness or high cost has kept you from prescribing any topical steroid...

THESE FACTS MAY CHANGE YOUR MIND

For complete details, consult latest Schering literature available from your Schering Representative or Medical Services Department, Schering Corporation, Bloomfield, New Jersey.

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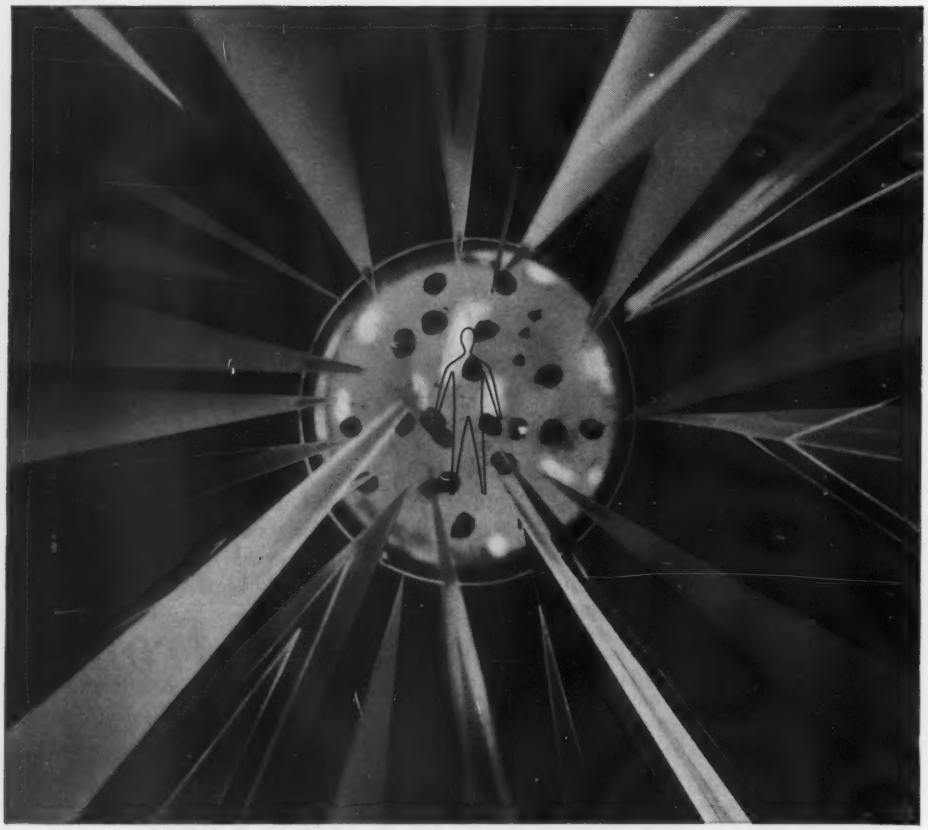

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because...it contains phosphate-potentiated tetracycline
for prompt, dependable broad spectrum antibacterial action.

because...it contains Fungizone, the antifungal antibiotic,
to prevent monilial overgrowth in the gastrointestinal tract.

Mysteclin-F resolves many respiratory, genitourinary and gastrointestinal infections—as well as such other conditions as cellulitis, bacterial endocarditis, furunculosis, otitis media, peritonitis, and septicemia. It combats a truly wide range of pathogenic organisms: gram-positive and gram-negative bacteria, spirochetes, rickettsias, viruses of the psittacosis-lymphogranuloma-trachoma group.

Available as: Mysteclin-F Capsules (250 mg./50 mg.) Mysteclin-F Half Strength Capsules (125 mg./25 mg.) Mysteclin-F for Syrup (125 mg./25 mg. per 5 cc.) Mysteclin-F for Aqueous Drops (100 mg./20 mg. per cc.)

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SQUIBB *Squibb Quality—the Priceless Ingredient*

Squibb Phosphate-Potentiated Tetracycline (SUMYCIN) *plus* Amphotericin B (FUNGIZONE)

THESE 128,000 PEOPLE IN MISSOURI NEED MEDICAL HELP

Heart disease, cancer, mental illness—everyone knows the nation's three major medical problems. Do you know that alcoholism ranks fourth? In the state of Missouri there are at least 128,000 alcoholics. These people need medical help. No one is in a better position to initiate and supervise a program of rehabilitation than the physician who enjoys the confidence of the patient or the patient's family.

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LIBRIUM

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During and after an acute alcoholic episode, Librium relieves anxiety, agitation and hyperactivity, induces restful sleep, stimulates appetite and helps to control withdrawal symptoms. The complications of chronic alcoholism, including hallucinations and delirium tremens, can often be alleviated with Librium.

During the rehabilitation period, Librium makes the patient more accessible, strengthening the physician-patient relationship. Librium therapy helps to reduce the patient's need for alcohol by affording a constructive approach to his underlying personality disorders.

Consult literature and dosage information, available on request, before prescribing.

LIBRIUM® Hydrochloride—7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide hydrochloride

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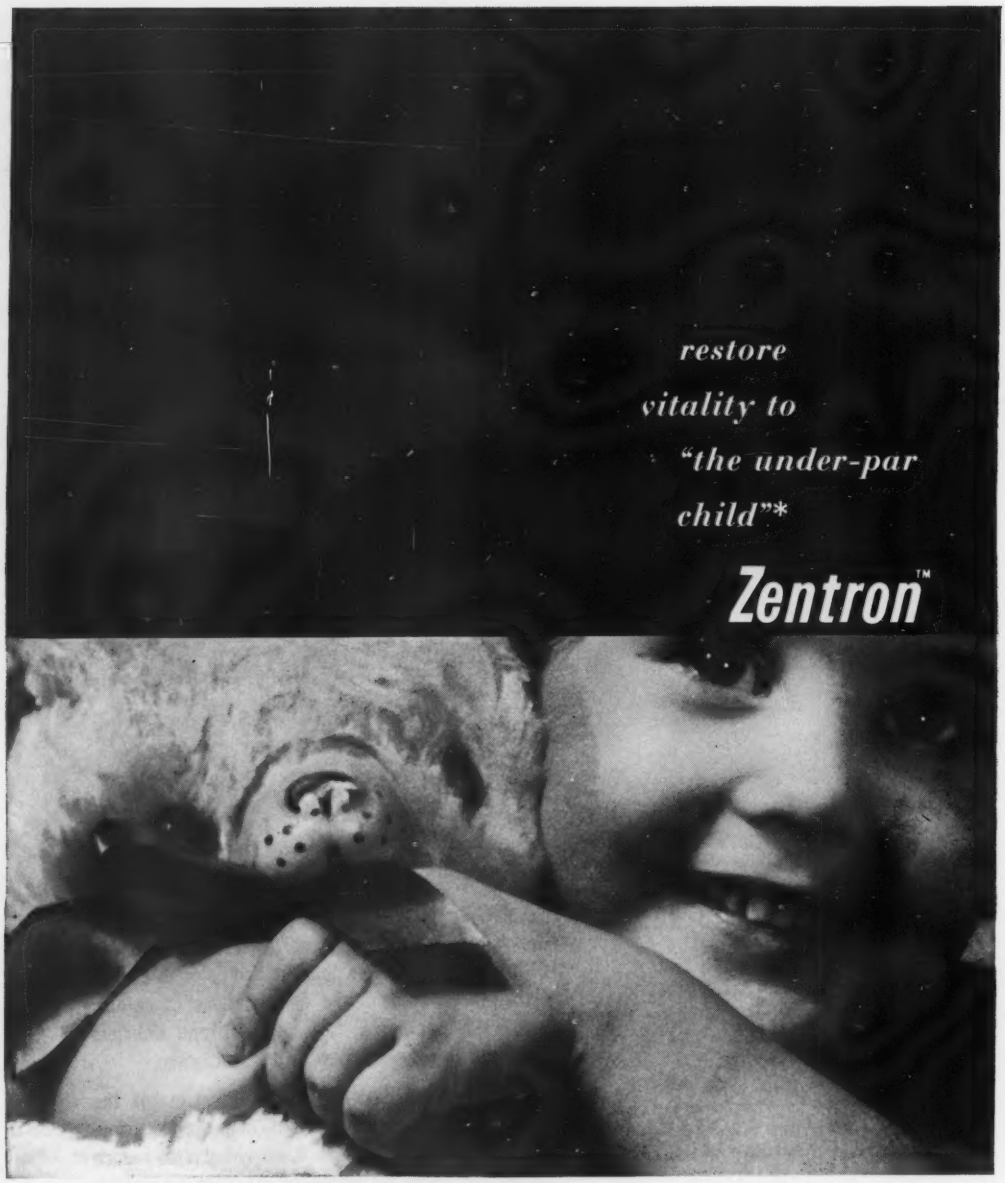


Zentron • comprehensive liquid hematinic

corrects iron deficiency • restores healthy appetite • helps promote normal growth

**underweight, easily fatigued, anorexic—because of mild anemia*

Each 5-cc. teaspoonful provides:

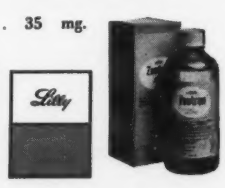
Ferrous Sulfate (equivalent to 20 mg. of iron)	100	mg.
Thiamine Hydrochloride (Vitamin B_1)	1	mg.
Riboflavin (Vitamin B_2)	1	mg.
Pyridoxine Hydrochloride (Vitamin B_6)	0.5	mg.
Vitamin B_{12} Crystalline	5	mcg.
Pantothenic Acid (as *d*-Panthenol)	1	mg.
Nicotinamide	5	mg.
Ascorbic Acid (Vitamin C)	35	mg.

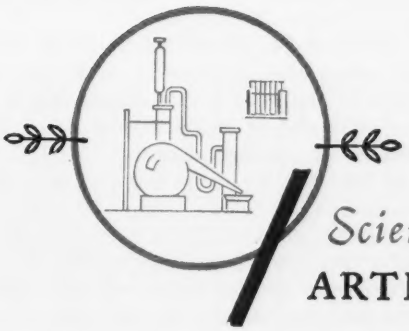
Alcohol, 2 percent.

Usual dosage: Infants and children—1/2 to 1 teaspoonful (preferably at mealtime) one to three times daily.

Adults—1 to 2 teaspoonfuls (preferably at mealtime) three times daily.

Zentron™ (iron, vitamin B complex, and vitamin C, Lilly) 119349





Scientific
ARTICLES

Lupoid Hepatitis

Report of Five Cases and a Review of the Literature

MANNY MOSER, M.D.,* ROBERT T. MANNING, M.D.**
and* MAHLON DELP, M.D.,† *Kansas City

Five cases of lupoid hepatitis from the University of Kansas Medical Center and twenty-nine cases collected from the literature are reviewed and reported. The etiology remains obscure but the pathogenesis likely involves an auto-immune mechanism. The most frequent clinical signs noted were jaundice, spider angioma, joint symptoms, hepatomegaly and splenomegaly. The laboratory findings are compatible with nonspecific liver injury.

Pathologic examination demonstrates severe liver alteration but no histologic evidence of disseminated lupus erythematosus. Patients with hepatic dysfunction and histological evidence of disseminated lupus erythematosus should not be reported as lupoid hepatitis. Lupoid hepatitis should probably be adopted as the logical diagnostic term in patients with hepatitis and a positive L.E. cell phenomenon.

"LUPOID HEPATITIS" refers to a somewhat ambiguous designation applied to a rather small group of patients with liver disease who are distinct for several reasons, but chiefly because of the demonstrability of the lupus erythematosus (L.E.) cell phenomenon. Mackay *et al.*[1] first coined the term "lupoid hepatitis" to denote such patients with active chronic hepatitis and the L.E. cell phenomenon. Joske and King[2] in 1955 reported the first two cases of hepatitis in which the L.E. cell phenomenon was observed.

In order to distinguish patients with lupoid hepatitis from those who have disseminated lupus erythematosus and associated hepatitis, Mackay and associates[1] used the term hepatic lupus to denote the latter group. Whether or not the appearance of the L.E. cell in association with hepatitis should be considered as a separate disease entity has not been clearly established.

Case Reports

This article is based on five cases of active chronic hepatitis with a positive L.E. cell phenomenon seen at the University of Kansas Medical Center, in addition to the twenty-nine cases reported in the literature.

The laboratory data are tabulated in Figure 1.

Department of Medicine, University of Kansas Medical Center.

Presented in part as Dr. Moser's Senior thesis.

* Intern, University of Kansas Medical Center.
** Associate in Medicine, University of Kansas Medical Center.
† Professor of Medicine, University of Kansas Medical Center.

The frequency of the reported signs and symptoms of the disease entity are recorded in Figure 2.

Case 1. K. S. M., KUMC No. 58-6394, a 17-year-old white woman entered the University of Kansas Medical Center on May 6, 1958 complaining of "gastric bleeding" of several months' duration.

She became jaundiced for the first time in September, 1956. Associated with this was a two-week history of migratory joint pain and swelling involving her knees, ankles and shoulders.

After November, 1956 she complained of frequent malaise, fatigue, nausea and intermittent jaundice. She was amenorrheic from September, 1956 to March, 1958 when she had one normal menses. From December, 1956 to the time of admission she had repeated episodes of epistaxis, bleeding from the roof of the mouth and hematemesis, for which she received a total of 20 units of blood. The patient was referred to the University of Kansas Medical Center for evaluation of a "bleeding disorder."

On admission she appeared well developed and well nourished but chronically ill. Positive findings included icterus, a few spider nevi on both upper extremities and slight increase in skin pigmentation. The liver was palpable 5 cm. below the right costal margin, the spleen 5 cm. below the left costal margin. A grade II systolic murmur was audible along the left sternal border.

Laboratory and X-Ray: See Figure 1, Case No. 30. Additional data: Blood ammonia 183 gamma per cent; BUN 4 mg. per cent; platelet count 86,000; complete clot retraction in 2 hours; prothrombin time 61 per cent of normal; bleeding time 60 seconds; coagulation time 13 minutes; macroglobulins were noted; cryoglobulins negative; an upper gastrointestinal series showed esophageal varices.

Because of the undoubted portal hypertension, esophageal varices and repeated hematemesis, a splenectomy and splenorenal shunt was performed on May 12, 1958. She tolerated the procedure fairly well. Postoperatively the white blood count rose to 33,000 and platelets to 350,000. Subsequently she had several episodes of gastrointestinal bleeding and a left hemothorax. Despite therapy, the patient's condition gradually deteriorated and, on the twenty-third postoperative day, she expired after five hours of hepatic coma and shock.

Autopsy showed postcollapse cirrhosis of the liver *(Figure 3),* 1000 ml. of ascitic fluid, hemosiderosis of the liver, pancreas and gastric mucosa, 2500 ml. left hemothorax, atelectasis of the left lung and an acute gastric ulcer. No histologic changes to suggest disseminated lupus erythematosus were found.

Comments: This case is a classical example of progressive chronic hepatitis in a young female with a positive L.E. cell test. No evidence of disseminated lupus erythematosus was present at autopsy. Splenectomy and splenorenal shunt failed to alter the progressive clinical deterioration.

Case 2. M. N., KUMC No. 58-15493, a 68-year-old woman entered University of Kansas Medical Center on November 9, 1958 complaining of "shortness of breath" of several months' duration and a nosebleed of one day's duration.

In July, 1958 the patient first noted unusual weakness and fatigue, followed shortly by the appearance of marked jaundice. She was hospitalized briefly and a diagnosis of infectious hepatitis was made. Subsequently she did fairly well until September, 1958 when she developed recurrent nausea, vomiting, shortness of breath and pedal edema. Digitalis and diuretics were given without apparent benefit. The symptoms progressed and she entered University of Kansas Medical Center for evaluation and therapy.

Physical examination revealed an acutely and chronically ill white woman who was very dyspneic at rest. Spider angiomata were present. Examination of the chest revealed dullness to percussion and decreased breath sounds in the lower half of the left chest, with scattered, moist rales throughout. Marked distention, a fluid wave and shifting dullness were present abdominally, as was generalized abdominal tenderness to palpation. Three plus pitting edema was evident to the knees bilaterally.

Laboratory: See Figure 1, Case No. 31. Additional laboratory data: Blood ammonia 87 micrograms per cent; prothrombin time 48 per cent of normal.

Strict bed rest and a low salt diet produced no effect on the edema. A paracentesis was done with removal of 2000 ml. of straw-colored fluid, following which she became confused and developed a gross tremor, most marked in the upper extremities. Her state of consciousness varied considerably; at times she was quite bright, alert and oriented, but more frequently she was grossly disoriented, confused and hallucinating. Terminally, electrolyte values were sodium 123 mEq./L., potassium 5.8 mEq./L., chlorides 75 mEq./L., and carbon dioxide 25.7 mEq./L.

She expired quietly on the thirty-third hospital day. Post-mortem examination revealed cirrhosis of the liver *(Figure 4),* 1500 cc. of ascites and 500 cc. of fluid in each pleural space. Multiple abdominal adhesions, hemorrhagic cystitis, esophagitis and focal mucosal ulceration of the stomach were also noted. There was no histologic evidence of disseminated lupus erythematosus.

Comments: This and the preceding case demonstrate progressive chronic hepatitis with a positive L.E. cell test and no histologic evidence to suggest disseminated lupus erythematosus. The only unusual factor noted was the second patient's advanced age. Most authors delineate lupoid hepatitis as being

most prevalent in young females, although some case reports are in the older age groups.

Case 3. K. L., KUMC No. 59-3301, a 16-year-old girl entered University of Kansas Medical Center on May 6, 1958 complaining of "jaundice" of eight months' duration.

Case No. bibl. No.	AGE	SEX	RACE	TSB	DSB	AP	TSP	SA	SG	SGG	CF	TT	TC	CE	SGOT	SI
1.[2]	37	F	W	1.5		16[Δ]	8.8	3.7	5.1	2.8	4+				27*	
2.[2]	21	F	W	3.0		32[⊙]	7.0	2.4	4.6	3.8	3+					
3.[3]	50	M	W	1.8		18[⊙]	8.3	3.3	5.0		4+	16	206	66.9		
4.[4]	33	M	W	7.9	3.0	9.1[□]	8.3	2.3	6.0		3+	17	232	72		
5.[4]	21	F	N	4.2			9.8	0.8	9.0	7.2	reg.	7.4				
6.[1]	20	F	W	5.0		21[⊙]	9.1	3.6	5.5	3.4	3+				30*	
7.[1]	21	F	W	4.8		22[⊙]	6.7	2.3	4.4	3.7	3+				65*	
8.[1]	29	F	W	3.5		8[⊙]	7.2	2.8	4.4	2.0	3+				70*	
9.[1]	66	F	W	0.6		17[⊙]	6.7	2.3	3.4	21	3+					
10.[1]	16	M	W	2.0		27[⊙]	7.4	3.2	4.2	3.0	3+				125*	
11.[1]	75	F	W	8.8		20[⊙]	7.3	1.9	5.4	2.6	3+					
12.[12]	19	F	W	2.7			13.1	3.7	9.4							
13.[10]		F	W						high							
14.[13]	29	F	W	6.0		37[⊙]	9.4	2.4	7.0	4.4					540	
15.[13]	19	M	W	14.0			8.4	3.1	5.3	3.7					302	
16.[13]	57	F	W	7.1			8.0	2.7	5.3	3.5					194	
17.[11]	39	M	W	8.0		31[⊙]	7.9	3.4	4.5	2.8						
18.[6]	24	F	W	2.24	1.8	44[□]	6.58	1.84		3.27		16	118	44		
19.[6]	23	F	W	29.6	21.6		7.18	2.27		3.15	4+	18				
20.[6]	39	F	W	1.10	0.84	15.[Δ]7	10.1	2.85		4.69	4+	13				
21.[6]	21	F	W	1.1	0.9	2.9[□]	10.0	1.3		7.34			179	65		
22.[6]	20	F	W	2.0	1.3	32[□]	10.55	2.77		6.0	4+	12	87			
23.[6]	45	F	W	9.2	6.5		8.03	2.96	5.07		4+	27	197			
24.[6]	55	F	W	5.3	5.04	18.[□]4	8.03	1.3		4.85	4+	18	111			
25.[7]	15	F	W	2.0			7.4	2.3	5.1							
26.[7]	28	M	W	0.6			6.8	3.2	3.6	1.9						
27.[7]	13	F	W	4.8			6.5	2.9	3.6	1.9					900	
28.[8]	32	F	W			12[⊙]	6.3	3.1	3.2		pos.	pos.				
29.[8]	21	F	W				10.7	1.7	9.0		pos.	pos.	110			
30.	17	F	W	2.3	0.9	2.9[Δ]	8.05	2.7	5.35		4+	66	128	66	143	145
31.	68	F	W	2.6	1.0	1.2[Δ]	5.36	1.86	3.50		4+	33	159	50	20	60
32.	16	F	W	23	15.5	3.5[Δ]	10.0	2.05	7.95		4+	38	94	15		80
33.	37	F	W	11.60	4.0	5.6[Δ]	5.65	2.86	2.79		1+		246	62	95	225
34.	46	F	W	3.5	1.7	7.3[Δ]	6.83	2.88	3.95		4+	64	221	39		360

Key:

TSB = Total serum bilirubin
DSB = Direct serum bilirubin
AP = Alkaline phosphatase
TSP = Total serum protein
SA = Serum albumen
SG = Serum globulin
SGG = Serum gamma globulin
CF = Ceph. flocc.
TT = Thymol turbidity
TC = Total cholesterol
CE = Cholesterol esters
SGOT = Transaminase
SI = Serum Iron

* = reported after original case report
□ = Bodansky Units
⊙ = King-Armstrong units
Δ = Mill. mol unit
▣ = Not given

Figure 1. Laboratory data.

She was asymptomatic until February, 1958 when excessive bleeding followed a tooth extraction. Subsequently she was generally well except for some malaise until July, 1958 when she first noted jaundice. She visited her physician for the first time in August, 1958. She was placed on restricted activity but was allowed to attend school in September. The jaundice and malaise persisted.

In January, 1959 she entered the local hospital for evaluation, at which time her skin was green-yellow in color, her stools were clay colored and urine was dark. She was referred to the University of Kansas Medical Center for further evaluation.

On admission she was a well-developed, well-nourished young woman in no apparent distress. The skin was markedly icteric and moderate acne was present. Palmar erythema and spider angioma were not evident. Examination of the abdomen revealed a firm, nontender liver edge 4 cm. below the right costal margin. The spleen was firm, nontender and 4 cm. below the left costal margin.

Laboratory and X-Rays: See Figure 1, Case No. 32. Additional data: Blood ammonia 97 gamma per cent; BUN 9.5 mg. per cent; creatinine 1.3 mg. per cent; prothrombin time 45 per cent of normal. X-ray examination demonstrated generalized bone demineralization. Esophageal varices were not present.

The patient was placed at bedrest and received a 1650 mg. sodium-60 Gm. protein diet. Forty mg. hydrocortisone in divided doses and 250 mg. chloraquin were given daily. The patient showed gradual clinical improvement, manifested chiefly by amelioration of the malaise and increased sense of well-being. She was discharged on bedrest and medications as noted above. The serum bilirubin was 16.8 mg. per cent at the time of discharge.

Comments: This patient demonstrates the clinical picture of marked liver disease with a positive L.E. phenomenon in a young female, without clinical evidence of disseminated lupus erythematosus. Correspondence with the family indicates the patient is improving at home.

Case 4. B. S. F., KUMC No. 58-10405, a 37-year-old woman entered the University of Kansas Medical Center on October 30, 1958 complaining of "weakness and an enlarged spleen" of several months' duration.

The patient was well until fifteen months prior to admission when she had an episode of nausea, vomiting, abdominal pain, acholic stools and jaundice. A diagnosis of infectious hepatitis was made and she was hospitalized for one month. Slow recovery occurred over a six-week period. The patient was rehospitalized with recurrence of jaundice five months later, and was found to have a pancytopenia and positive L.E. cell phenomenon. She continued to have intermittent symptoms of nausea, vomiting, abdominal pain and jaundice, and was referred to the University of Kansas Medical Center because of the persistent pancytopenia.

Physical examination on admission showed a well-developed, moderately well-nourished woman who appeared pale but in no distress. Abdominal examination revealed moderate right upper quadrant tenderness, but no hepatomegaly was noted. The tip of the spleen was palpable on deep inspiration but was not tender. One plus pretibial pitting edema was present with associated nonpitting swelling of the ankles. Several ecchymotic areas were present over the thighs.

Laboratory and X-Ray: See Figure 1, Case No. 33. Additional data included platelets 16,000. No esophageal varices could be demonstrated on an upper gastrointestinal series.

The clinical impression was postnecrotic cirrhosis of the liver with hypersplenism and pancytopenia. A shunt procedure was felt to be inadvisable because of the marked thrombocytopenia. Liver function studies at this hospital remained normal, with a total serum bilirubin of 0.7 mg./100 ml., serum albumin of 3.45 Gm./100 ml., serum globulin of 2.27 Gm./100 ml., alkaline phosphatase of 1.4 millimol, bromsulphthalein 10 per cent retention, and thymol turbidity of 3. The clinical course was unchanged from admis-

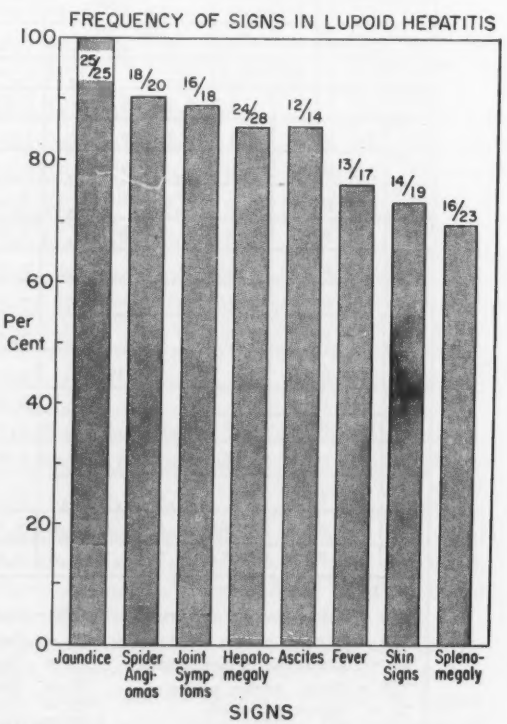


Figure 2. Frequency of signs and symptoms in lupoid hepatitis.

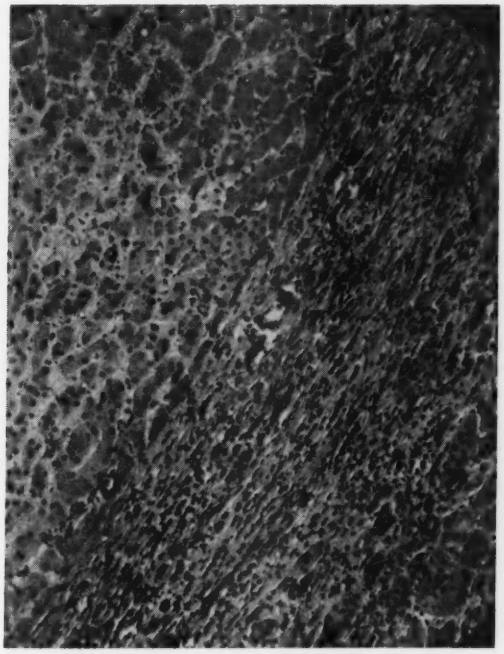


Figure 3. Liver tissue at autopsy, Case No. 1.

sion. The patient was discharged on a 60 Gm. fat diet, 10 mg. hydrocortisone b.i.d., 5 mg. folic acid t.i.d., and 1000 micrograms vitamin B_{12} weekly.

She subsequently expired at home following recurrence of bleeding and ensuing hepatic coma. An autopsy was not obtained.

Case 5. M. B., KUMC No. 59-8815, a 46-year-old white woman entered the University of Kansas Medical Center on June 11, 1959 complaining of intermittent swelling of the fingers, wrists, knees, ankles and shoulders with an associated recurrent jaundice.

She was first hospitalized two weeks in October, 1958 for "hepatitis," manifested by severe nausea, vomiting, dark urine, light-colored stools and icterus. Associated with the "hepatitis" was mild painful joint swelling. From October, 1958 to June, 1959 intermittent nausea, vomiting, jaundice and increasingly severe joint swelling with pain were present. She was referred to the University of Kansas Medical Center for further diagnostic work-up and treatment.

On admission she appeared well developed and obese but not in distress. The sclerae were mildly icteric. There were no spider nevi or pigmentary changes noted on examination of the skin. Abdominal examination revealed the liver to be three finger-breadths below the right costal margin, firm and tender. The spleen and kidneys were not palpable. Positive findings of the extremities were limited to swelling of the feet and ankles bilaterally with slight tenderness.

Laboratory and X-Ray: See Figure 1, Case No. 34. Additional data: Leucine aminopeptidase 190; platelet count 243,000; prothrombin time 91 per cent of normal; bleeding time 30 seconds; clotting time 13 minutes. Liver biopsy showed moderate portal fibrosis with slight cellular regeneration. X-ray revealed no esophageal varices or bone lesions.

She was placed at complete bedrest with 1400 calorie, 1650 mg. sodium-40 Gm. fat diet with essentially no clinical change. The laboratory values, as noted in Figure 1, Case No. 34, did not change during her hospitalization. She was discharged on 10 mg. hydrocortisone b.i.d. every other day, bedrest and the diet described above. She has been followed in the out-patient clinic for six months and has slowly improved. The joint symptoms, nausea, vomiting and icterus have been minimal. The hepatic function studies demonstrate improvement, with the total serum bilirubin dropping from 6.6 mg./100 ml. to 2.9 mg./100 ml.

Comments: This case demonstrates a more bizarre clinical picture with definite rheumatoid arthritis, in addition to the progressive liver disease with the L.E. cell phenomenon. Others have described the same diffuse protean symptoms in their cases of active chronic liver disease with a positive L.E. cell test.

Discussion

Etiology and Pathogenesis:

The etiology and pathogenesis of lupoid hepatitis have not been elucidated and continue to be controversial.

The primary lesion in the two cases reported by Joske and King[2] was believed to be an active chronic viral hepatitis, and the L.E. cell phenomenon was in some way a sequela of the hepatitis. They did not believe they were dealing with primary disseminated lupus erythematosus since this disease does not produce the gross changes in liver structure observed in their cases.

Demonstration of the L.E. cell phenomenon usually indicates disseminated lupus erythematosus, but Bettley[3] feels that it is not pathognomonic. He also notes that L.E. phenomenon is associated with gamma globulin abnormality, and the L.E. cells found in lupoid hepatitis might be linked with the consistent gamma globulin changes seen in this group of patients. He suggested that the findings of myelomatosis in his one case might have been partly responsible for the production of the L.E. phenomenon.

Heller *et al.*[4] suggested the L.E. cell phenomenon in these patients represents a false-positive test, and the phenomenon may have an immunologic basis.

L.E. cells are not obtained in the blood of patients with hepatic cirrhosis even with very high serum globulin values, but Sherlock[5] states they have been noted in the cirrhosis occurring in young girls with

adrenocortical overactivity. She feels it may be a specific disease or merely a variant of posthepatitic cirrhosis.

Mackay *et al.*[1] were of the opinion that parenchymal cell damage might be the initiating factor of an auto-immune phenomenon in this group of patients. Hepatic cell protein, released via cell necrosis or injury, is postulated to act as an antigen and thus stimulate antibody production. Such antibodies are "anti-liver" and produce further damage upon combination with hepatic cell protein. Such a process would be cyclic and, unless interrupted, would lead to progressive liver cell injury. This concept is nonspecifically supported by the finding of high levels of gamma globulin in patients with lupoid hepatitis. Recent developments in fluorescent tagging of antibodies should provide confirmation or refutation of this hypothesis.

Bartholomew and coworkers[6] expressed the opinion that the cases reported had many features in common with the present concept of diffuse lupus erythematosus, and that these findings were foreign to any current concept of primary liver disease. They were unable to rule out the possibility of two disease entities superimposed, and indicated that until a specific test for the virus of hepatitis is perfected this possibility must not be discarded.

Lupoid hepatitis and lupus erythematosus may be distinguished as separate entities by clinical findings and pathological changes as concluded by Mackay and his group.[7] However, overlapping features in the two groups suggests a similar pathogenesis, possibly mediated via an abnormal auto-immune mechanism with destruction of host tissues.

Lupoid hepatitis and disseminated lupus erythematosus are believed to have a common immunologic basis, as noted by Hutchings and Wigley,[8] but may have a separate etiology.

A viral etiology was proposed in ten of the thirty-four case reports, and alcohol was felt to be the initiating factor in one case. There was no mention as to specific etiology in the remaining cases.

Signs and Symptoms:

The most frequent symptoms and signs observed in patients with lupoid hepatitis are listed in Figure 2. Bartholomew and cohorts[6] are of the opinion that the clinical symptoms found in their patients are not compatible with liver disease alone. They frequently noted sun sensitivity, pleuritis, arthritis, thrombophlebitis and transfusion or drug reactions. Such signs and symptoms are recorded infrequently in other case reports. It should be noted that one of their patients had a histological diagnosis of disseminated lupus erythematosus, and two others had suggestive evidence.

Of the skin manifestations reported, acnes or atypical rashes have appeared frequently. The arthralgia observed is not infrequently seen with viral hepatitis, but not so frequently as in lupoid hepatitis. The other signs observed are commonly seen with liver disease of all types.

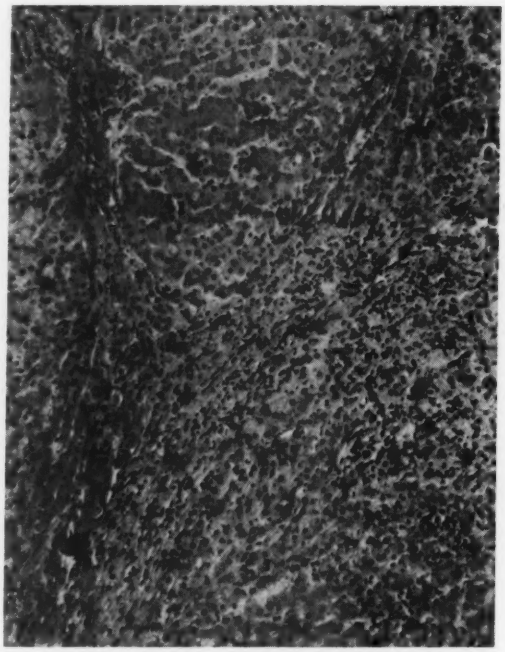


Figure 4. Liver tissue at autopsy, Case No. 2.

Laboratory:

Biochemical studies in patients with lupoid hepatitis reveal fairly constant abnormalities such as elevated total serum bilirubin, decreased serum albumin, elevated serum globulin, especially the gamma fraction, positive cephalin flocculation test, and elevated serum glutamic oxaloacetic transaminase activity. These are, of course, nonspecific indications of liver injury.

Six patients had a positive serologic test for syphilis and three others a positive Coombs' test. These findings, in addition to a consistently elevated serum gamma globulin, are suggestive of an immunologic disorder as noted by Mackay *et al.*[7]

Kofman and his group[9] studied serum and liver biopsy specimens in twenty-five patients with disseminated lupus erythematosus, concluding that the apparent hepatic dysfunction represented (in most patients) an abnormal plasma protein pattern rather than actual hepatic parenchymal abnormalities.

Post-mortem Findings:

Autopsies, with histological studies, have been recorded by several observers.

The first autopsy (Case No. 3) was reported by Bettley[3] on a patient with lupoid hepatitis. Post-mortem examination confirmed the diagnosis of multinodular cirrhosis. Particular attention was directed to the possibility of systemic lupus erythematosus, but no evidence was found.

The autopsy findings were reported by Heller *et al.*[4] in a case of lupoid hepatitis, and the histological sections demonstrated subacute hepatic necrosis with cirrhosis formation. There was no pathological evidence consistent with disseminated lupus erythematosus.

Kidney biopsy (Case No. 6) and autopsy (Case No. 9), reported by Mackay's group,[1] showed changes in the glomerular capillary walls similar to that seen in disseminated lupus erythematosus.

Wilkinson and Sacker[10] reported post-mortem findings (Case No. 13) of portal cirrhosis, but no evidence of systemic lupus erythematosus.

Cirrhosis and chronic ulcerative colitis at necropsy in a questionable case (Case No. 17) of lupoid hepatitis was demonstrated by Gray *et al.*[11] No evidence of disseminated lupus erythematosus was found.

In Cases No. 18, No. 19 and No. 23, reported by Bartholomew and associates,[6] autopsies were done; and a kidney biopsy in one (Case No. 22). Histological changes in Case No. 19 were compatible with a diagnosis of disseminated lupus erythematosus. In two other cases (Cases No. 18 and No. 22), there were definite vascular changes in the kidney, but no conclusion was drawn as to their compatibility with a diagnosis of disseminated lupus erythematosus. In Case No. 23, no mention was made in regard to the histological sections of the kidney or in other tissues.

Mackay *et al.*[7] presented two more autopsies in cases of lupoid hepatitis (Cases No. 25 and No. 27), but no statement was made about the post-mortem findings to suggest disseminated lupus erythematosus.

The autopsy findings in Cases No. 30 and No. 31 in this series gave no evidence to suggest disseminated lupus erythematosus even after a concentrated effort to demonstrate such lesions.

Histological changes in the liver were studied by Mackay and coworkers[7] in nineteen patients with hepatic dysfunction in disseminated lupus erythematosus. Minor changes were noted in most of the cases, and nodular cirrhosis was found in two patients. One patient with such cirrhosis did display the clinical and biochemical features of active chronic hepatitis.

From autopsy and biopsy reports it is clear that many patients with lupoid hepatitis have no histological evidence of disseminated lupus erythematosus. Patients with histological evidence of disseminated lupus erythematosus should not be included in the category of lupoid hepatitis.

Acknowledgments

We wish to express our sincere thanks to Dr. Sloan J. Wilson, Dr. Arthur P. Klotz and Dr. Robert W. Weber of the University of Kansas Medical Center staff for use of their cases in this report.

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Editor's Note: This article was submitted to THE JOURNAL for publication in March, which is the University of Kansas Medical Center issue. Due to space limitations at that time, THE JOURNAL was able to publish only half of the articles submitted.

The remaining papers will appear in the upcoming issues. THE JOURNAL would like to thank these authors for being so patient while waiting for their article's publication.

Not a tenth of us who are in business are doing as well as we could if we merely followed the principles that were known to our grandfathers.—*William Feather*

It may be that the race is not always to the swift, nor the battle to the strong—but that's the way to bet.—*Damon Runyon*

A parliament is nothing less than a big meeting of more or less idle people.—*Walter Bagehot*

Tracheotomy

The Problem of Decannulation of Tracheotomized Patients

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MANY PAPERS ABOUT TRACHEOTOMY have been written. In some of them decannulation is often considered, or at least pointed out, but few discuss the problems that arise concerning patients with indwelling tracheotomy cannulas, on whom a decision must be made regarding removal of the tracheotomy tube.

In the laryngological field this problem has been widely discussed, mostly related to decannulation after the diverse laryngeal procedures. This information is extremely useful for managing primary laryngeal problems, but is insufficient for other cases on whom tracheotomies have been performed for other indications.

The care of the latter cases is primarily that of the otolaryngologist, but it may be necessary at some time for anyone in the medical profession to have to perform a tracheotomy. Thereafter, the problem of decannulation will become apparent.

For anyone performing a surgical procedure it is essential not only to understand the procedure, but to know how to evaluate correctly the indications and the limitations of technique, the prognostic data, and possible complications of the procedure itself.

If the procedure is an emergency, the performer's responsibility can be limited to the early recognition of the problem and his immediate action should be directed toward counteracting, relieving or bypassing the obstacle. When these steps are carried out properly and on time they will resolve the immediate problem; nevertheless, it is not until the complete resolution of the problem is reached that we can say that the patient has received the maximal benefit from treatment.

This last point will be the basis for our judgment in regard to the degree of normality, compensated normality or modified normality that the patient will experience thereafter.

This paper is an attempt to point out some of the basic clinico-physiological facts upon which decannulation should be based.

General Consideration

The primary consideration in decannulation is the fact that it is an individual problem. A descriptive account of individual cases will be insufficient to outline the general consideration of the problem. On the other hand, as has been previously stated, decannulation should always be considered on an individual basis.

The only way to reconcile these two statements would be by realizing the substratum of the problem. From that the basic ideas will emerge, and in the transformation of these ideas to practical principles the answers for individual cases will be obtained.

- **In this article the importance of following specific indications in every case of decannulation of a tracheotomy patient is stressed.**
- **It is necessary to have a basic knowledge of the physiopathology and systemic relationships of the respiratory system before decannulation.**
- **The combination of this knowledge with the direct study of the case itself will yield proper indications for the procedure.**
- **Decannulation is a medical accomplishment because it yields restoration of normality, and in some cases, complete health of the patient.**

Decannulation is intimately related to pulmonary ventilation. It is on the understanding of the physiopathology of this function and its systemic relationships where the practical principles for decannulations are to be obtained. By definition, the volume of air in liters breathed by an individual is called pulmonary ventilation. One tenth of this volume reaches the alveolae. This air provides O_2 to the alveolar capillaries and removes the CO_2 released by the same vessels. In a simple obstruction of the respiratory tract, the primary physiological change observed is a reduction in the ventilatory capacity of the pulmonary bellows. Due to this impairment of O_2, saturation of the blood decreases, giving origin to anoxemia and tissue anoxia. In contrast, the CO_2 in the blood increases, giving origin to hypercapnea.

Hypercapnea produces an increase in free carbonic acid in the blood phenomenon known as respiratory

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acidosis. Respiratory acidosis, if sustained, leads to metabolic acidosis.

Each of these disturbances by itself, if severe enough, can cause tissue damage and death.

Gray, in his paper about the physiology of respiratory obstructions, was able to correlate the different magnitude of these phenomenon in relation with the degree of obstruction. For the purpose of demonstration his experiment, with some modification, was repeated.

The dog was elected as the experimental animal, for its anatomy was familiar, and the available facilities for its care were superior. The dog was placed under light anesthesia of sodium nembutal. The hypopharynx and larynx were anesthetized with 5 per cent cocaine solution. This was followed by the insertion of a fitting endotracheal tube. The femoral artery and vein were surgically exposed and No. 18 polyethylene tubes were inserted to obtain repeated blood samples. Thereafter, the endotracheal tube was obstructed in about 10 per cent of its diameter. Ten minutes later arterial blood samples were obtained and O_2, CO_2 and Ph were determined. Following this same pattern of experimentation the obstruction of the tube was increased to 20, 30, 40, 50 and 60 per cent. Each of these obstructions was followed by sampling arterial blood. Figure 1 illustrates the magnitude of the changes encountered in the saturation of O_2, CO_2 and Ph in relation with the degree of obstruction.

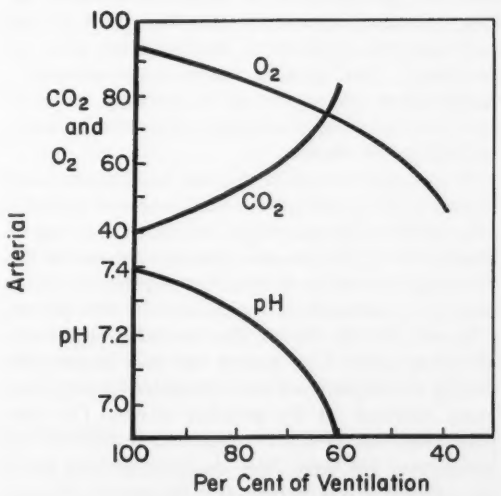

Figure 1.

Since the pulmonary ventilation is the algebraic sum of the partial effects of the separate agents, the logical approach to the removal of a tracheotomy tube is when these separate agents reach normality or its neighborhood. At that point, tracheotomy has rendered its maximal benefits and the tube must be removed.

The condition of the pulmonary parenchyma is of extreme importance regarding decannulation. Gaseous interchange in the lungs may be hindered not only by obstruction of the larynx, trachea or bronchae, but also by spasm of the smooth muscles of the bronchae by the presence of fluid in the alveolae (alveolitis edema), by decrease in the respiratory surface caused by pulmonary collapse (pneumothorax), compression of the lung (pleural effusion), inflammatory processes (pneumonia), obstruction of a pulmonary blood vessel (infarct), or by loss of elasticity of the pulmonary parenchyma (emphysema).

In these cases a tracheal cannula aids ventilation by decreasing the amount of work of the respiratory system by reducing the distance (dead space), in which the air column must move.

Until now we have analyzed the effectiveness of respiration. Another factor intimately related to decannulation is the analysis of respiration as work. In this, the factor of time has to be abolished and the consideration will lean toward the mechanical part responsible for this function.

Respiratory movements are the resultant of muscular vectors. Their evaluation is decisive for decannulation and the inspiratory muscles, as well as the expiratory muscles, are of equal importance. The hypo, or inactivity of the inspiratory muscles, will produce hypoventilation. The inefficacy of the expiratory muscles will cause impairment of the cleansing function of the respiratory tract, and will likewise reduce ventilation. When both mechanisms are operative and assure some margin of reserve for ventilation, decannulation should be performed.

Respiratory muscular activity, like any other biological activity, should be analyzed from the point of view of its origin, regulation, transmission and action. Respiratory muscles are under voluntary and involuntary control. The former, like other cortical function, in certain circumstances is apt to simulate a pathological condition that does not exist organically. For example, one of the problems of decannulation encountered in infancy and childhood is that in which the child has conditioned himself by breathing through tracheotomy, and in spite of good respiratory function through normal airway, developed apnea and other symptoms as soon as the tube is obstructed. Even if breathing can be stopped voluntarily for a certain time, never long enough as to produce death by asphyxia, this demonstrates that cortical control of respiration is limited.

The most important neural factor of respiration is the respiratory center. It is located on the floor of the fourth ventricle and responds automatically to nervous or humoral stimuli.

In neurological diseases or cerebral trauma in which

this center is involved, the time for decannulation will be indicated by the first signs of regression of the neurological disturbance. Encephalitis, bulbar poliomyelitis, cerebral palsy, etc., fall into this category. Muscles of the pharynx and tongue, under certain pathological circumstances, will obstruct the airway by the double mechanism of reducing the lumen and by poor handling of secretions. Signs such as adequate deglutition will help decide when to decannulate these cases.

The laryngeal muscles which form part of the airway and modify the airway itself are of capital importance in considering decannulation. With regard to laryngeal muscles, usually good phonation after obstruction of the tracheotomy stoma, and in some cases an endoscopic examination, are enough to determine when a tracheotomy tube should be removed.

Most of the involuntary mechanism of the pharynx and larynx responds to a sensitive stimulus. Important reflexes, such as cough reflex, can be abolished if the sensitive component of the arch is hindered. So, the assurance of a normal sensitivity will help carry out a successful decannulation.

Tracheotomy itself can involve some complications that can interfere with decannulation. The presence of subcutaneous emphysema, the level at which tracheotomy was performed, the length and caliber of the tube, can, under certain circumstances, create differences in this procedure. In cases in which tracheotomy is performed for the avoidance of the positive pressure exerted in the vascular system by cough, as in some cases of cardiac and vascular surgery, decannulation can be carried out when the patient shows clinical evidence of vascular and cardiac compensations.

Case Reports

The following description contains random cases of tracheotomy and decannulation seen by the Department of Otorhinolaryngology at the University of Kansas Medical Center.

Case No. 1. C. S., KUMC No. 58-3817. Eight-month-old white male, admitted to the pediatric service with the complaint of intermittent spells of gasping respirations and cyanosis. These episodes started one week before admission. Consultation was requested to the Department of Otorhinolaryngology. On initial examination it was noted that the patient had normal ventilatory functions as well as deglutition and phonation. During his stay in the hospital he developed a sudden episode of respiratory obstruction and cyanosis and was resuscitated after mouth-to-mouth breathing. The child recovered and was well for a few days until a similar episode occurred. At that time it was necessary for insertion of a bronchoscope for the ventilatory obstruction to cease. Tracheotomy was performed and the patient did well thereafter.

On this admission several endoscopic and x-ray studies were secured in the attempt to discover the etiology of the obstruction, but the results were inconclusive. Due to the fact that this baby was successfully operated upon a few hours after birth for a tracheogeal fistula, where according to the operative record, "A fistula was resected from the upper middle third of the esophagus to the bifurcation of the trachea," it was accepted that tracheomalacia was the causative factor for the episodes of obstruction.

After instructing the parents about tracheotomy care the child was discharged to their care. Two tracheotomy tubes of the same caliber were given to them to take to the physician for the weekly exchange of cannulas.

Three months later the patient was re-admitted for further studies. New endoscopic examinations did not reveal evidence of intrinsic obstruction of the airway, and possible extrinsic obstructions were ruled out by clinico-radiological studies.

Decannulation was started in a progressive fashion: first, by using progressively smaller tubes until the smallest caliber was reached, second, by obstructing the opening of the tube. No evidence of hypoventilation was encountered, and the patient was discharged with a taped "00" tracheotomy tube.

After ventilating normally for three weeks the child was again admitted for final decannulation. The tube was removed, and for two days the baby did well until the morning of the third day when he developed a final episode of respiratory obstruction. At that time re-insertion of tracheotomy tube and immediate artificial respiration were without avail, and the patient died.

In autopsy a diverticulum of the trachea was found located at the site of bifurcation, a remnant undoubtedly of the tracheoesophageal fistula. It was easy to demonstrate in the specimen that the inversion of this diverticulum into the trachea was responsible for the respiratory obstructions experienced by the patient.

Case 2. W. P., KUMC No. 59-5372, 3½-month-old white male. This patient was seen in consultation by the Department of Otorhinolaryngology after being admitted on the pediatric service. The complaint was that of fever, cough and respiratory embarrassment for three days' duration. During initial examination it was obvious that the patient was suffering respiratory obstruction. Laryngeal stridor and chest retraction were marked and rales in either pulmonary field were present. The baby was immediately placed in a croupette and started on systemic antibiotics. After several hours of observation it was appreciated that the signs of hypoventilation were

more marked, and tracheotomy was done. After five days the baby was well, without temperature, and the lungs were radiologically clear. An attempt was made at that time to tape the tracheotomy but the child immediately became apneic and the tape was removed. Trying to rule out mechanical obstruction, several laryngoscopies were performed, all of which proved to be inconclusive. After three weeks of futile attempts at decannulation it was observed that the baby went into episodes of apnea only when he was awake, and the tracheotomy tube was taped. He tolerated the taped tracheotomy perfectly well when asleep. It was decided that the apneic reaction was being produced by a conditioned reflex that the child had on the tracheotomy tube. To satisfy this reflex the tracheotomy tube was removed when the patient was asleep, and the silver plate of this cannula was left tied around the neck. A few days later it was possible to remove the plate entirely. Since that time, the baby has done well.

Case No. 3. N. P., KUMC No. 56-1967, 6½-year-old white male. In 1956 this subject was diagnosed as having pseudohypertrophic, progressive muscular dystrophy. Since that time, the patient had been admitted 21 times suffering from pneumonia. On each admission bronchoscopy had been required.

Fourteen months ago he was admitted with pneumonia. On admission it was appreciated that the respiratory muscles were barely capable of carrying on the effort of ventilation and incapable of producing the extra effort needed in coughing. Bronchoscopy and tracheotomy were performed. The patient did well and was discharged, and since that time hospital admissions have not been required.

In the preceding descriptions it is possible to analyze different cases on whom tracheotomies were performed following diverse indications. The reason for tracheotomy is objectively described, and the different aspects presented for decannulation are recorded. It may be noted that most of them followed different indications for decannulation and required different pre-decannulation studies. This emphasizes the previous statement that decannulation should be considered on an individual basis. It is also apparent that it is indispensable for one to understand the concepts of pulmonary physiology in health, as well as in disease.

Conclusions

As in tracheotomy, decannulation of a tracheotomy patient is basically a matter of clinicophysiological indications. To follow indications in this regard is as important and as necessary as the indications for which the tracheotomy was performed. Each decannulation should be considered individually, but the knowledge of the general concepts of ventilation and pulmonary functions and their pathological manifestations in disease is necessary for the arrival of these conclusions *(Figure 2)*.

A practical and useful rule to follow in a case of decannulation is to divide consideration and examination above and below the site of tracheotomy. Not until the case is reviewed and these three sites considered, should decannulation be performed. It is absolutely indicated to leave an indwelling tracheotomy tube when the indications for decannulation are not present or are not clear.

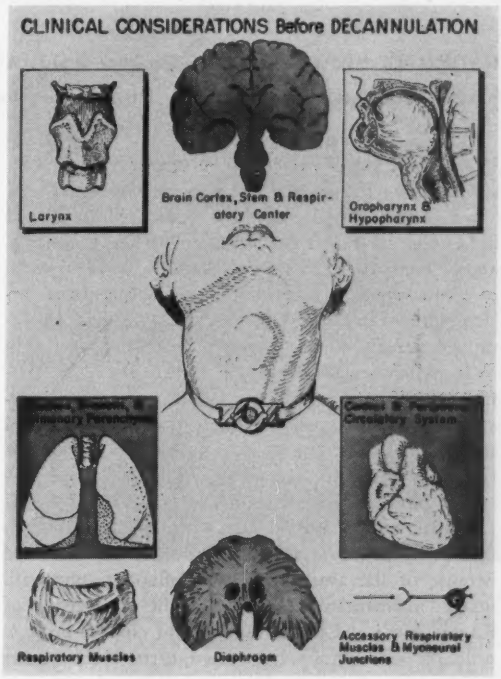

Figure 2.

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Speech

The Evaluation of Speech Mechanisms

RALPH L. SHELTON, JR., Ph.D.; WILLIAM M. DIEDRICH, Ph.D.; KARL YOUNGSTROM, M.D., Ph.D., *Kansas City*

THE EVALUATION OF SPEECH DISORDERS involves appraisal of the speech mechanism, assessment of other factors which influence speech learning, and description of the acoustic phenomena which are produced. Knowledge of the relationship between structure and speech is important to the practicing physician who may be asked to examine speech handicapped persons so that medical problems interfering with speech learning may be identified and, if possible, resolved. Certain information pertaining to examination of the speech mechanism is presented; and employment of radiography, which has been used in phonetics research and in the study of voice and speech physiology since shortly after the discovery of Roentgen rays,[12] is emphasized. Recently interest in utilization of radiography in speech has increased because of the availability of cinefluorography with image intensification.[9, 13, 17] At the University of Kansas Medical Center research and clinical projects utilizing radiography have been carried out or are underway in the areas of esophageal speech and cleft palate speech.

Equipment

The principal item of equipment used in these studies is a cinefluorographic unit composed of a tilting x-ray table which has a 150 kv undertable tube, 0.3 and 1.2 mm focal spot, an x-ray generator of 300 ma at 150 kvp capacity, a nine inch image intensifier, a sixteen millimeter magnetic sound cine camera which is operated at 24 frames per second, and a dynapulse. The latter provides bursts of x-ray of one to two millisecond duration which are synchronized with the opening of the camera shutter so that radiation is generated only when the camera shutter is open. This equipment makes possible cine recording at acceptable levels of x-ray exposure to the patient. The nine-inch image intensifier permits visualization of the adult speech mechanism from the lips to the posterior pharyngeal wall and from nasopharynx to trachea. Lateral spot films are made to supplement the cine material.

Cinefilm analysis is done by use of a film editor, sound reader, regular motion picture projector, and a variable speed, reversible projector. The latter may be used with a tracing cabinet.[5]

From the Department of Hearing and Speech and the Department of Radiology, University of Kansas Medical Center, Kansas City, Kansas. The study of post-laryngectomy speech is supported in part by a research grant from the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare, Washington, D. C. The cleft palate research program is supported by the National Society for Crippled Children and Adults, Inc. Equipment for these and other studies has been provided by the organizations mentioned and by the National Institutes of Health and the Kansas Division of the American Cancer Society.

Radiography is a tool that supplements other testing procedures and has both clinical and research application in the resolution of speech defects. Problems of esophageal voice and cleft palate speech are discussed.

Esophageal Speech

The laryngectomized person may learn to produce sounds for speech by voluntarily taking air into the esophagus and pushing it out as one would during eructation. Many writers[1, 4, 11] have stated that constriction at the level of the cricopharyngeus, which is located at the junction of the pharynx and esophagus, serves as a pseudolarynx. As air is moved through this narrowed lumen *(Figure 1)*, it is set into vibration, and sound is thus produced.

The site and morphology of the pseudolarynx in post-laryngectomized speakers is being investigated at the University of Kansas Medical Center by radiographic procedures. Spot and cinefluorographic films have shown constriction in the cricopharyngeal area simultaneous with voice in some subjects. However, in other subjects different sites of constriction have been observed. Thus the cricopharyngeus or other muscle fibers may be utilized in producing an esophageal voice. The extensiveness of the carcinoma and the resulting surgical procedure are probably the most important determinants of the postoperative morphology of the pharyngeal-esophageal tract. Other factors, however, such as infection or previous x-ray treatment may also affect the form and function of the pseudolarynx. Radiographic analysis of the pseudolarynx during phonation has shown great differences in the size and shape of the contracting fibers.

In Figure 2, subjects A and B show constriction for phonation of what seems to be the fibers of the cricopharyngeus. The vibrating tissues in subject C, however, appear to be higher than the level of the cricopharyngeus. Fibers of the inferior constrictor muscle may be involved. Subject D illustrates a long pseudolarynx which is probably composed of middle and inferior pharyngeal constrictor fibers.

Apparently laryngectomees with poorly defined or long areas of constriction *(Figure 2, subjects E and F)* have difficulty producing sound. However, some good speakers have a long constriction; therefore, this length is not the only factor in the production of good voice. For example, factors apart from the pseudolarynx such as senility, motivation, and hearing loss may be important.

The value of professional speech teaching in the rehabilitation of the laryngectomized person cannot be overemphasized. Such persons need careful evaluation and instruction if a new voice is to be developed. The International Association of Laryngectomees recently reported the results of a questionnaire mailed to more than 7,000 laryngectomized persons.[6] Of the 4,800 who responded, 75 per cent had learned to speak again by using esophageal speech exclusively. Three out of four who were using post-laryngectomized speech, however, experienced difficulty in its use. The reasons for failure and difficulty were not given, but in some instances lack of professional teaching may be presumed to have contributed. A few laryngectomized speakers have become so-called "lay" teachers. Operating without professional education, supervision, or knowledge of the many variables involved in speech learning, these persons may sometimes be detrimental to their clients. At this institution a number of laryngectomized persons who are excellent speakers serve as highly valued volunteer assistants to the teaching staff. By relating their own speech learning experiences, they serve a morale-building function and help to orient the newcomer to the speech learning process. In a monthly meeting they work directly with the teachers in conducting lessons. The staff plans all instruction, however, and provides individual lessons to beginning speakers once or twice a week.

Cleft Palate Speech

Patients at the cleft palate clinic are evaluated by specialists in audiology, dentistry, otolaryngology, plastic surgery, radiology, and speech pathology. Utilization of radiography in the speech evaluation will be discussed here.

Speech evaluation of cleft palate clients involves assessment of both articulation and voice. In normal speech, the palate is elevated during production of all sounds except the nasalized m, n and ng (ing). When speech tests indicate that problems are present,

Figure 1. A radiograph of a laryngectomized person phonating the vowel "ah." The arrow indicates the constriction of muscle fibers which is called the pseudolarynx. In this subject the pseudolarynx extends from the level of the lower margin of the fourth cervical vertebra to the level of the lower margin of the sixth cervical vertebra.

determination must be made whether or not they are caused by lack of contact between the muscular palate and the posterior wall of the pharynx. Such a deficit may cause certain articulation problems and/or nasal voice quality. Palatopharyngeal approximation may be assessed cinefluorographically or by use of spot radiographs of the subject at rest and during sustained phonation.[3] The vowel *ee* as in f*ee*t is especially useful for this purpose since it is the vowel most apt to be nasalized.[15] During its production the tongue fills much of the anterior portion of the mouth thus directing the air against the area of palatopharyngeal closure. In phonation film, an adequate palate will usually appear in contact with the posterior pharyngeal wall. The extent of palatal movement from the neutral or rest position can be observed whether or not contact is made.

Additional tests of the palatopharyngeal sphincter should be made. Oral breath pressure as measured manometrically is used to reveal escape of air through the nasopharynx via air passages not recorded in the x-rays. If the client can produce as much oral breath pressure with the nares open as with them pinched

closed, the palatopharyngeal mechanism is probably adequate.[16] Manometric measures should be used in conjunction with radiography in that spuriously high pressure ratios may be obtained by contraction of the nares or less obviously by creation of pressure in the front portion of the mouth even though palatopharyngeal closure is incomplete. Thus the radiographic and manometric procedures supplement one aonther.

Palatopharyngeal inadequacy is also indicated by certain patterns of articulatory error. Workers at the University of Iowa have constructed a pressure articulation test to evaluate speakers' ability to produce those sounds which best discriminate between adequate and inadequate palatopharyngeal closure.[10] Intelligibility of the plosive sounds p and b is related to palatopharyngeal competency,[18] and several studies have indicated that persons with cleft palate are more likely to misarticulate sibilants (s, z, etc.) than other sounds.[2, 7, 14]

The clinical utility of radiography in palate evaluation is illustrated in Figure 3. The subject, a twelve-year-old boy with a congenitally short palate, demonstrated a compensatory forward movement of the posterior wall of the pharnyx. Cinefluorography indicated that each time his palate was elevated the posterior wall was moved forward to meet it. Nevertheless, closure was incomplete. This coordinated movement of palate and pharyngeal wall in speech is remarkable because it does not usually occur. When first seen, the boy made articulatory errors on the s, z, and l sounds, and his voice was moderately nasal. With speech lessons, which were conducted over a period of six months, he learned to produce the defective sounds correctly except for occasional distortion. Some nasality remained, however, and the client reported that he had to be continually careful to avoid gross speech error. Because of these continuing problems, a pharyngeal flap was performed. His speech and voice problems and his self-consciousness about speech were resolved without additional instruction.

Ratings of nasal voice quality are found to be related to measures of articulation deficiency.[8, 19] Thus the more severe the articulation problems in cleft palate speakers, the greater is the likelihood that trained observers will report the presence of nasality. This finding suggests that reduction of articulation

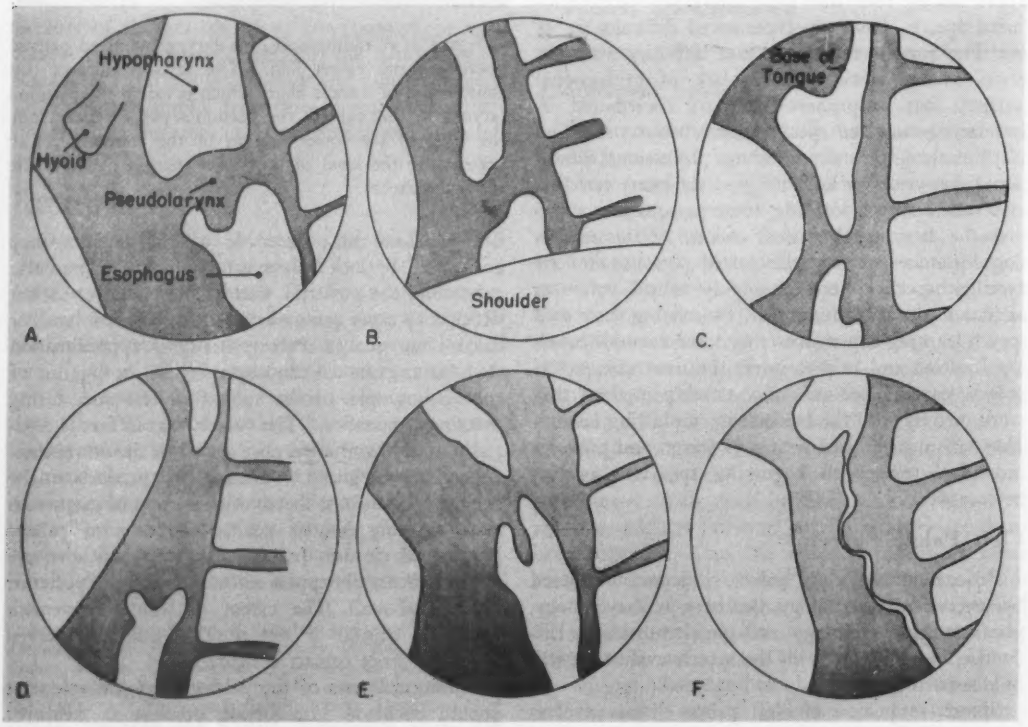

Figure 2. Cinefluorographic tracings illustrating differences in the morphology of the pseudolarynx during phonation in six different persons. Subjects A, B, and C were good speakers; D was a fair speaker, and subjects E and F spoke poorly. The latter subject had a pharyngectomy in addition to laryngectomy.

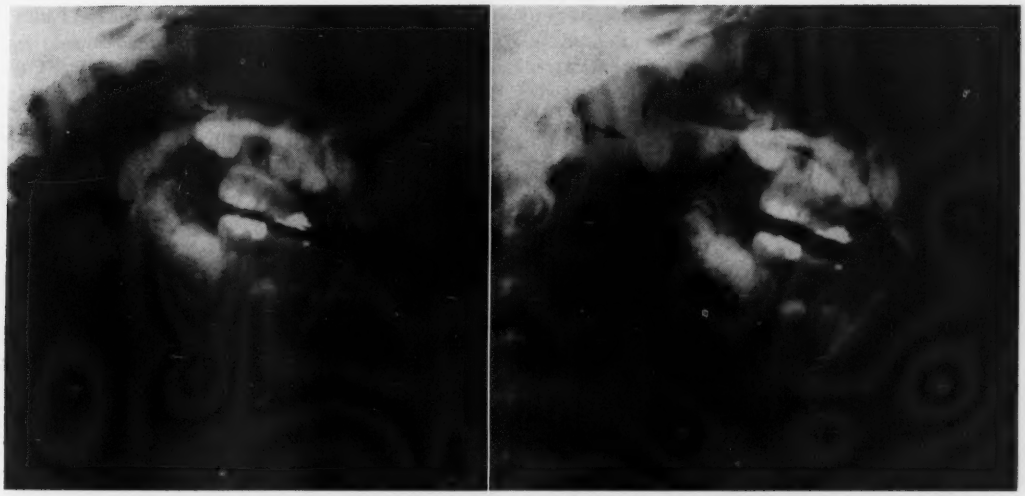

Figure 3. Radiographs of a twelve-year-old boy who had a congenitally short palate. On the left, the subject is shown during quiet breathing. On the right, the same subject is phonating the vowel *ee* as in *feet*. The large arrow indicates a forward movement of the posterior pharyngeal wall; however, as indicated by the small arrow, palatopharyngeal closure was not complete. Comparison of the two films shows that some palatal movement did occur. Note that during the phonation film the tongue fills much of the oral cavity.

deficiency is more fundamental than attention to nasal voice quality for cleft palate speakers. Successful repair of the palatopharyngeal mechanism, which may be accomplished surgically or prosthetically,[2] will facilitate development of articulation even though speech instruction frequently is needed to help the client learn to produce sounds correctly. Articulation errors in persons with adequately repaired mechanisms are amenable to remedial speech instruction whereas speech lessons in the presence of inadequate palatal structure are much less satisfactory. Successful repair will also result in reduction or elimination of nasal voice quality.

Summary

The use of radiography in the study of speech phenomena has been discussed with particular reference to the disorders of laryngectomy and cleft palate. Better understanding of the physiology of speech mechanisms and improved management of speech disorders can be accomplished when radiographic procedures are employed.

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Medical HISTORY

The Origin and Development of Autopsy

M. GENE REED, ***Wichita***

In the gloomy wood and stone anatomical theatre the candle light glinted on the scalpel as three hundred pairs of eyes watched the blade dissect the corpse's cranial nerves. The air reeked of sweat, leather and putrefying flesh. High upon the gradients, jostled on all sides. . . .
(Padua, 1598)

Definition

IN MODERN TERMINOLOGY the words "autopsy" and "post mortem" are used interchangeably. The word "autopsy" is of Greek derivation and, translated loosely, means to see with one's own eyes. Applied to medicine, it means to dissect a dead body to determine what brought about death. "Post mortem," of course, means after death.

Obstacles in Development

For centuries there was great reluctance to open the bodies of the dead. It is said that even Hippocrates had a horror of contact with corpses, lest the spirit of the deceased haunt him. This great master felt that anatomy was indeed the foundation of medicine but believed that one could learn it from open wounds. The Roman law of Galen's time (162 A.D.) prevented the use of human cadavers for the study of anatomy. In India, opening the body after death was forbidden by religion. An old Hebrew tenet, "He that toucheth the dead body of any man shall be unclean for seven days" restrained the Jews from any post mortem procedure.

Whether from traditional, religious, legal, or aesthetic motives, these objections prevented any advancement in medical knowledge for centuries.

Editor's Note: M. Gene Reed is the wife of Dr. D. Cramer Reed of Wichita. Mrs. Reed wrote "The Origin and Development of Autopsy" as an English class thesis while working toward a degree.

Events Leading to First Autopsy

"Historically, the adoption of the practice of autopsy examination marks the division between primitive and modern medicine."

Human interiors were certainly inspected by the early Egyptians. During centuries of elaborate embalming procedures, the "taricheutes" eviscerated bodies and prepared them for the tomb. (According to Dr. Ibanez—fifty centuries and fifty million corpses!) In spite of this widespread practice, no knowledge of anatomy was transmitted by this civilization.

It is generally accepted that the Romans did no dissecting of the human body. Galen, the great compiler of ancient anatomy, dissected only apes and lower animals and based his conclusions of human anatomy on these findings.

In the 3rd century B.C., anatomical dissections were performed in Alexandria for the first time in medical history. This is particularly interesting in light of the classic Greek attitude toward dissections. While they venerated their dead far too much to allow such a procedure, they fostered it in a conquered realm. These operations opened the door to the conclusion that diseases originate in various organs, rather than in any mysterious humours. Unfortunately, the practice had a relatively short life and was eventually prohibited. There is an interim of one thousand years before it appears again.

Autopsies Begin

Spiro reports that "after the sixth century autopsies were occasionally performed in Byzantium to learn the cause of plagues." However, little was known about autopsies until the latter part of the thirteenth century. According to Dr. Krumbhaar, the first known medico-legal autopsy was performed by William of Saliceto (1201-1280) and his notes would indicate he had performed others.

In 1286 a physician of Cremona opened many bodies for the express purpose of discovering the cause of the pestilence which was sweeping the country. During the plague of 1347 the Pope ordered post-mortems to find the cause of that disease.

Dr. Major writes that the first coroner's inquest was reported in 1302. A certain nobleman was believed to have been poisoned, and the court ordered a post-mortem. Bartolome de Varignana, a professor of medicine at the Anatomical School of Bologna, performed the autopsy and verified the suspicions.

One of the most famous teachers and physicians of the University of Padua was Gentile de Foligno. He is credited with one of the earliest recorded autopsies in 1341, on which occasion he found a gall stone.

In 1410 Pietro dI Argelata carried out an autopsy on Pope Alexander V who had died suddenly and mysteriously.

These and other examples show that the autopsy method was gaining precedence and power during the Middle Ages.

Milestones

In the latter part of the fifteenth century, the first book on pathological anatomy was written by Antonio Benivieni and it correlated symptoms of disease with findings at autopsy.

In Florence, another "first" was recorded in that same period. A post-mortem was performed for the sole purpose of discovering if the disease was of a hereditary character.

Vesalius, of Padua, provided one of the landmarks in medical history with his *Fabrica* in 1555. Medicine could progress no further without an accurate understanding of the structure of the body. The unorthodox *Fabrica* supplied this knowledge. The book aroused much controversy because it dislodged the medical halo of Galen.

"Vesalius' tragic end was hardly a just reward for his monumental contribution. He was dissecting, with full consent of the relatives, the body of a Spanish grandee, and as he cut into the heart, the muscle gave a feeble contraction . . . (which is not uncommon in those recently dead). This was reported to the court of the Inquisition, and Vesalius was sentenced to death. . . ." (Guttmacher)

The study of anatomy reached its zenith in Italy in the last part of the 16th century. There were thousands of students and beautiful anatomic theatres, particularly those at Padua and Bologna. The zeal soon spread to other European countries.

Much of the human dissection for the next one hundred fifty years was done in behalf of art by physicians and artists in collaboration, notably Michelangelo and Realdus Columbus, Da Vinci and Della Torr', and Von Calcar and Vesalius. Their work greatly advanced the study of human form and musculature, and, of course, anatomic illustration.

Very little is written on the progress of pathological anatomy for almost a century. Physicians had become engrossed with two new problems—syphilis and gun shot wounds.

That autopsies were still being carried on was indicated in an interesting report concerning William Harvey:

> "In the year 1635, there lived in the county of Shropshire one yeoman called Thomas Parr, reputed to be 152 years old. When his fame reached the ears of the Lord Thomas Howard, Constable of England, he was brought to London on a litter. There he was wined and dined, and in short order died. King Charles I commanded his personal physician, one William Harvey, to perform an autopsy on the remains of Old Parr. This was duly done, and Dr. Harvey pronounced all the organs of the deceased to be healthy and sound. It was noted that there was not even calcification of the costal cartilages. As no anatomic cause of death could be found, Old Parr was adjudged to have died of a surfeit. . . ." *(M.D.,* June, 1957)

In 1673 Van Leeuwenhoek, of Holland, developed the microscope. Although he observed a large number of bacteria, he did not relate them to disease. Another century was to pass before this momentous connection would be made.

Theophile Bonet, 1679, pursued the study which Benivieni had started two centuries earlier. In three large volumes he compiled a record of every known disease, with symptoms and pathological data—some 3,000 protocols.

The close of the 17th century saw pathology established as a science, and the next century witnessed constant advances in pathologic observing.

Often called the father of anatomy, Giovanni Morgagni contributed one of the imperishable books of medicine, *De Sedibus et Causis Morborum,* published in 1761. This important work contained a vast array of pathological findings, arranged and indexed, preceded by minute histories, symptoms, therapy and the relationship of the laboratory findings to the clinical picture.

The 19th century marks the beginning of modern medicine when autopsy reached its full development.

In 1801 Dupuytren wrote his treatise on pathological anatomy based on his observation of 1,000 autopsies.

Passionately devoted to his work was the pathologist, Bichat. It was said that he frequently slept at the morgue. During one winter he performed more than 600 post-mortems. His important work was *Anatomic Générale,* published in 1801. Previous writers had discussed individual organs. Bichat's description of the various systems of the body had a profound effect on clinical medicine. This amazing pathologist introduced the technique whereby tissues

obtained at autopsy could be preserved for future microscopic study.

Bichat influenced other French physicians, especially Corvisart, who used the autopsy to study the development of disease and made diagnoses from laboratory findings. He instituted routine autopsies at the College de France, and as Sigerist reports:

> "Immense was the delight of the doctor and his pupils if this confirmed the diagnosis. Still more instructive, however, were instances in which discrepancies arose. They gave Corvisart an opportunity of showing, in masterly fashion, how and why he had erred and of explaining what was to be learned from these new observations." (Farber)

Undoubtedly, the most prolific pathologist was Carl Rokitansky of Vienna. During his 48 years at the Pathological Institute, "the number of autopsies performed by him or by assistants under his direction had reached the astounding number of 59,786! In addition . . . there were at least 25,000 medico-legal autopsies!" (Major) His autopsy techniques, though modified, are still followed today.

While Dr. Major considers Morgagni the father of pathology, Saphir and Farber feel that this role belongs to Virchow. In 1858 Virchow wrote one of the great books of medicine, *Cellular pathologie*, which presented a revolutionary concept—the fundamental role of the cell. It was his theory that sickness was a result of diseased cells. "Morgagni had pointed out the importance in pathology of an organ as the seat of disease; Bichat had called attention to the importance of tissues; now Virchow pointed out the fundamental role of the cell." (Major) This theory is today the basis of the cancer concept.

"Beginning with Vienna in 1806, chairs of pathologic anatomy were rapidly established in many countries, cooperation with hospital deadhouses established, autopsies abounded and medical teaching and progress prospered." (Krumbhaar) The British and Irish were quick to follow the developments on the continent, and a wealth of information was gained from autopsy. Even more important, the ground work was laid for future revelations.

Although the microscope had been a potential ally for over a century, it remained for Pasteur and Koch "to excite new interest into Van Leeuwenhoek's 'little animals' and usher in an exciting period in modern medical history." (Major) As a result of their discoveries, bacteriology was to dominate the last quarter of the 19th century.

Robert Koch demonstrated Pasteur's germ theory in diseases and developed the laboratory techniques necessary to prove their etiology. Among the pathogenic agents discovered by Koch were: the anthrax and tubercle bacilli, cholera vibrio and ophthalmus bacillus.

The close of the 19th century saw other microorganisms identified and demonstrated. The microscope became a great boon to the science of autopsy.

Development in America

Although somewhat belated, the history of the autopsy in America followed a similar pattern and reflected teachings of the various homelands.

Benjamin Franklin was one of the instigators of the first medical school, now known as the University of Pennsylvania, which was founded in Philadelphia. The first class graduated in 1768. Major tells us that a member of the faculty, Philip Physick, was kept busy with post-mortem studies of victims of the yellow fever epidemic of 1793.

Even earlier autopsies are reported in the New World. Hektoen writes of the autopsy of the double human monster in San Domingo in 1533. This operation was authorized by the church "to determine whether one or two souls should be baptized . . . each would have been a beautiful woman."

In 1605 and 1606 members of Champlain's group on Ste. Croix Island and at Port Royal were victims of scurvy. During the second year twelve of the forty-five died.

> Our surgeon, named Des Champs, of Honfleur, a man skilled in his profession, opened some of the bodies to see if he could discover the cause of this illness better than those who had tried the previous year. He found the same parts of the body affected as in those opened on Ste. Croix Island and could discover no remedy for curing them, anymore than had the others. (Kektoen)

These studies were truly amazing when we consider that in Europe at the corresponding period, post-mortem examination was in its earliest stages.

The first medico-legal autopsy in the colonies was done in 1691 on the body of Governor Slaughter of New York. Only four times previously had other autopsies been performed.

Although medicine was not well-developed in America, two works on pathologic anatomy were written here in the early 1800's. William Edmonds Herner wrote a treatise on pathology in 1829. Ten years later Samuel D. Gross, of Philadelphia, published a textbook of pathology, "the first exhaustive treatise on pathological anatomy in the English language." (Major)

By the middle of the 19th century America was producing its own medical scientists and, with their contributions, the prestige of American medicine was becoming established. In just a century this country would replace Vienna as the mecca of medical science.

In 1905 one of the most fascinating autopsies in history was performed. It is of especial interest because it was done 113 years after death had occurred.

John Paul Jones, of "Don't give up the ship" fame, had been buried in France. When the United States ambassador learned that the little cemetery was to be uncovered in a slum-clearance project, he tried to find the remains of the naval hero.

> "Three weeks of exploration disclosed five lead coffins, one of which was believed to contain his remains. By a meticulous process of elimination, a body fitting that of Jones in all details was found. The body was is remarkably good condition. Although there was no evidence that it had been embalmed, there was a strong odor of alcohol about it. . . . Two anthropologists and historians were responsible for the decision that the autopsy was performed on the right body. The correlation of the known clinical history with the findings at autopsy enabled the examiners to conclude that the body was that of John Paul Jones." *(Physician's Bulletin,* 1958)

Current Status and Role

Today there are few restrictions on autopsies. The general rule is that the next of kin has the right of burial, and, accordingly, the right to grant or withhold an autopsy.

At present there are two schools of thought regarding the current and future roles of autopsy. In 1956 Dr. Isaac Starr wrote a controversial article on the values of autopsy today. He declared that post-mortems had become routine and burdensome; that the emphasis on pathology denied the existence of mental and emotional disorders; that no therapeutic advances had come from that school; and that preventive medicine was ignored.

The opposing school was righteously indignant and, led by the eminent Dr. Cannon, lashed out immediately and vigorously. "The autopsy is becoming more important today mainly because we are in such an unusually active period of chemical, hormonal and isotopic therapy; and the final evaluation of most of these newer forms of treatment must come from post-mortem findings."

It may be that the post-mortem has already made its chief contributions to medical science and, indeed, that it has become routine. But just as from other procedures which have become routine, such as a complete blood count, other observations and discoveries can be made. For only by such a procedure can we measure the effectiveness of new advances in the treatment of cancer, leukemia, collagen diseases and other unsolved mysteries. Only from such procedures can we furnish adequate explanations for unexpected deaths. So long as diseases alter the various structures of the body, the autopsy will remain a valuable adjunct to medical science.

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Headaches, Secondary Amenorrhea and Progressive Failure of Vision

Case Presentation

A 29-YEAR-OLD WHITE WOMAN was admitted for the first time to KUMC complaining of failure of vision of about two years' duration. Two months before admission she noted the sudden and rapid deterioration of vision in both eyes, particularly the left one, and she could no longer read a newspaper.

She had had two normal pregnancies, the first one at age 17 and the second at 25. Following her second pregnancy she had been amenorrheic until the present admission. When she was 16 years old she began to have headaches which were diagnosed as migraine, and when she was 23 she was seen in the medicine and neurology outpatient clinics where the diagnosis of migraine was confirmed. The patient said that nervousness seemed to precipitate her headaches, and a typical migraine attack would begin with scintillating scotomata, either straight ahead or in the upper visual fields, followed by a large, central, "clear" scotoma. Afterward she developed a "dreamy" state in which she was conscious and could walk, talk, hear and carry on a conversation but in which a peculiar quality of familiarity existed (*deja vu* phenomenon). She had a tingling sensation in her hands, usually in the left hand. She had nausea and frontal or unilateral headache. With the inception of her second pregnancy she had had no further episodes of migraine until the night before her admission.

Her mother had had severe headaches, but otherwise her family history was non-contributory.

The patient was a slightly obese, white woman who was alert and active, and who seemed to be in no apparent distress. Her blood pressure was 117/70; her pulse was 80 and regular. A right carotid systolic bruit was heard in the neck. All of the deep tendon reflexes were hypoactive, and the visual acuity was 20/40 in the right eye and less than 20/100 in the left eye. There was a minor superior temporal quadrant defect in the right eye and a nearly complete temporal hemianopia, probably involving the macula, in the left eye. She was righthanded. Otherwise the neurological examination was "negative."

A voided urine specimen showed a heavy trace of albumin and 25 to 30 pus cells per high power field. The hemoglobin was 11.8 gm. per cent. A white count was 7,550 with 53 per cent polymorphonuclear neutrophiles, 39 per cent lymphocytes, 1 per cent eosinophiles and 7 per cent monocytes. The mean corpuscular hemoglobin concentration was 31.4. The serology was non-reactive. The serum sodium was 143 mEq/L; potassium, 3.7 mEq; chloride, 106 mEq; calcium, 2.7 mEq; bicarbonate, 28.0 mEq; and phosphorus, 5.2 mEq. The fasting blood sugar was 72 mg. per cent with hourly glucose tolerance values of 72, 106, 59 and 63 mg. per cent. There was no glycosuria. At 8:00 a.m. the circulating eosinophile count was 150 per cubic millimeter. Three and one-half hours after she received 20 units of ACTH intramuscularly, the eosinophile count was 88 per cubic millimeter. The urinary 17-ketosteroids were 9 mg. and 17-hydroxysteroids were 9.1 mg. per 24 hours. An electroencephalogram was normal. The I-131 thyroidal uptake was 19 per cent in 24 hours.

An operation was performed on the eighth hospital day. The systolic blood pressure did not drop below 110 mm. of mercury during the entire 4-hour procedure. She was given 500 ml. of bank blood. Immediately upon recovery from anesthesia she had a profound left hemiplegia with a left Babinski sign. The pupils were small and equal and reacted to light. She would squeeze her right hand on command, but she would not speak. Three and one-half hours after

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completion of the operative procedure a lumbar puncture was performed because of continued left hemiplegia. The spinal fluid was moderately bloody with a pressure of 300 mm. Four hours after operation she would hold up two or three fingers of her right hand as directed, but she would not open her eyes or speak. Ten hours after operation the left hemiplegia was still present, and she no longer responded to commands. Her right hand and foot moved aimlessly. Her blood pressure remained stable throughout the postoperative period. The urinary output was satisfactory. Twelve hours after operation the right pupil appeared to be larger than the left. The respiration became periodic, and a right Babinski sign was present. The surgical wound was reopened, and further surgery was done. She remained comatose and gradually developed hypotension. Her pupils became dilated and fixed. Twenty-three hours after completion of the initial operation all cardiac and respiratory actions ceased.

Dr. Mahlon Delp (moderator): Are there any questions?

Josephine Anderson (fourth year medical student):* Will you describe her headaches in more detail?

Dr. Keith Whitaker (resident in neurosurgery):** There seemed to always be a typical train of events associated with her headaches. They were not always unilateral, and I believe that they were more frequently bi-frontal.

Miss Anderson: What kind of attack did she have just before admission?

Dr. Whitaker: She had a typical migraine attack which was exactly the same as those she had experienced up to the period five years before her admission.

Frank Chesky (student): Did she have any stiffness of her neck?

Dr. Whitaker: No, she did not.

Ivan Carper (student): Had she always been obese, or did she develop obesity after the onset of her symptoms?

Dr. Whitaker: She was not markedly obese; she was just an average plump young housewife.

Herbert Curran (student): Did she cease to lactate after the birth of her second child?

Dr. Whitaker: Her breasts remained large after the last delivery and up to the present time, and she had had intermittent lactation during the past several years. I do not believe she nursed her last baby.

Mr. Carper: Did she have a history of polyuria?

Dr. Delp: She had had polyuria and polydipsia of one month's duration about four months before she was first seen here.

Hugh Cox (student): What was the specific gravity of the urine on admission?

Dr. Delp: It was 1.016.

Melvin Cheatham (student): Was there any acromegaly?

Dr. Whitaker: No, there was not.

Mr. Curran: Was a catheter specimen obtained on the first urine?

Dr. Whitaker: No.

Mr. Chesky: Was a blood urea nitrogen value obtained?

Dr. Whitaker: No.

Mr. Cheatham: Were any other calcium or phosphate levels reported?

Dr. Whitaker: No, they were not.

Mr. Carper: Did the patient make any attempt to speak following surgery?

Dr. Whitaker: I do not know whether she attempted to talk or not; no one ever heard her say a word.

Mr. Curran: Will you describe the eyegrounds on admission?

Dr. Whitaker: They were normal, although there was some question about the possibility of temporal pallor.

Dr. Robert Hudson (internist): Before her admission did the transient weakness or tingling of her hands ever occur after the headache formed?

Dr. Delp: The tingling sensation occurred with the onset of the headaches or as a premonitory sign of their onset.

Dr. Robert Manning (internist): Was there any evidence of metastatic calcification or cataracts?

Dr. Whitaker: No.

Dr. Manning: Were any of her symptoms suggestive of tetany?

Dr. Whitaker: No.

Dr. Manning: Did she complain of numbness around her mouth?

Dr. Whitaker: No.

Dr. Delp: May we have the x-rays now, please, Mr. Cheatham?

X-rays

Mr. Cheatham: On admission a PA view of the skull shows no bony abnormalities of the cranial vault. The frontal sinuses appear to be clear, and there is no calcification of the pineal body. The most significant finding in the lateral view is the tremendous enlargement of the sella turcica which measured about 14 x 21 mm. on the regular films *(Figure 1)*. The posterior clinoid process is poorly defined.

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* Although a medical student at the time of this conference in April, 1959, she, like the others referred to as students, received the M.D. degree in June, 1959.

** Although a resident in neurosurgery at the time of this conference in April, 1959, he is now captain, Medical Corps, Lackland Air Force Base.

Figure 1. Lateral view of skull taken on admission.

A carotid arteriogram done two days before surgery shows normal filling of the internal carotid artery to the carotid siphon on the right side. The anterior cerebral artery does not fill well. Of most significance is the lateral shift of the carotid siphon away from the midline *(Figure 2)*. The lateral view shows essentially the same findings with normal filling of the carotid siphon. The middle cerebral artery fills well throughout its distribution. Again, the filling of the anterior cerebral artery is probably not normal.

Another internal carotid arteriogram done four hours postoperatively shows the bone flap turned for a right fronto-parietal craniotomy. On the left side there is filling of the internal carotid artery, some filling of the middle cerebral distribution, and the anterior cerebral artery appears to be well outlined. There is shifting toward the left possibly indicating increased pressure on the right. There is partial filling of the internal carotid artery on the right, but there is no filling of the rest of the vascular distribution. A thrombosis or pressure may have been exerted on the artery, or, possibly, a spasm may have caused the artery not to fill any farther.

A lateral film four hours after surgery shows filling of the right internal carotid artery and into the right external carotid. Most of the vessels are filling from the external carotid. The internal carotid narrows progressively until there is no more filling of the middle anterior distribution.

Dr. Delp: I believe that the patient's death was not anticipated. Mr. Chesky, will you give us your primary diagnosis and your opinion as to the immediate cause of death?

Differential Diagnosis

Mr. Chesky: This 29-year-old woman was admitted here with the complaint of failure of vision over a period of two years. She had a history of migraine headaches. She had had amenorrhea for four years following the delivery of her second child. Because of the progressive failure of vision and certain questionable laboratory findings, my initial diagnosis is an expanding lesion either in the sella or suprasella area of the cranium.

Sarcoid granuloma, gumma, amyloidosis and tuberculosis of the pituitary can be dismissed because of the lack of history and physical findings and because of the negative laboratory values.

Metastatic carcinoma of the pituitary is a possible diagnosis, but it is a rare disease and can be ruled out because of the duration of the patient's illness, and because there was no evidence of primary carcinoma.

Meningioma of the tuberculum sellae initially can cause visual manifestations and pressure atrophy of the pituitary, but I shall dismiss it as a primary diagnosis because of the negative x-ray findings.

Thirty-five per cent of intracranial aneurysms occur between the ages of 21 to 40. They are seen specifically in the anterior communicating artery, the anterior cerebral and the internal carotids, and remain silent in the vast majority of cases. Those which are not ruptured may cause symptoms of visual field

Figure 2. Carotid arteriogram taken two days before surgery.

loss or of extraocular muscle paralysis, neither of which was present in this patient.

Eosinophilic granulomas cannot be completely dismissed, although there was no evidence of acromegaly, a condition which is usually present in that disease.

My final diagnosis is chromophobe adenoma. This is a slow-growing tumor and the most frequent of pituitary adenomas. Its early manifestation is usually gonadotrophic failure which may be manifested by secondary amenorrhea. Visual defects occur in the bitemporal fields as the tumor expands. In our case a glucose tolerance curve was low, and there were borderline values in the Thorn test and the I-131 uptake study, all of which is compatible with chromophobe adenoma. The thyroid and adrenal functions are often not eliminated until several years after the onset of the disease, and that, together with the x-ray findings of ballooning of the sella turcica, substantiates the diagnosis. Twenty per cent of chromophobe adenomas are cystic. Hemorrhage into the cyst could account for the sudden diminution of vision two months before admission. In regard to the correlation between the amenorrhea and the second delivery: chromophobe adenomas can grow during pregnancy. It is my assumption that the patient underwent surgery to have a hypophysectomy. The left hemiplegia may have been the result of vascular spasm or thrombosis during the operation, and there may have been diffuse infarction of the cerebral hemisphere. The edema manifested itself by the progression of diminution of the sensorium, dysesthesia, and aimless movements of the right arm and leg. Pressure on the brain stem may possibly have been due to herniation over the tentorium with resultant pupillary signs, respiratory involvement, hypertension and death.

Clinical Discussion

Dr. Delp: Thank you, Mr. Chesky. Four months before admission the patient had had polyuria for about one month, but she had no polyuria when she was seen here as an outpatient or three to four weeks later when she returned as an inpatient. How do you explain that, Mr. Cox?

Mr. Cox: A hemorrhage into the tumor with pressure on the posterior hypophysis could cause a relative diuresis by obstruction of the antidiuretic hormone release. Although it may have been only temporary as a transient episode of diabetes, I believe that an acute expansion of the pituitary gland would be the most likely cause.

Dr. Delp: What is your explanation, Miss Anderson?

Miss Anderson: Hemorrhage into a cyst could have increased the pressure in the area of the hypothalamus, and could give rise to a transitory diabetes insipidus. Also at that time there was retrogression of the eye signs.

Dr. Delp: It was reported that the patient had intermittent lactation. Her finger size increased because her rings became too tight, and she had to wear a larger glove. How do you interpret that, Mr. Carper?

Mr. Carper: An eosinophilic adenoma could cause acromegaly which would be the only evidence of such a process. Such a tumor could be histiologically diagnosed as a chromophobe one.

Dr. Delp: Mr. Cox?

Mr. Cox: Fifteen cases were reported in which there was evidence of acromegalic features without frank acromegaly in lesions of the pituitary. Three of the cases were diagnosed as chromophobe adenomas secreting lactogenic hormones.

Dr. Delp: It was reported that the patient had alterations in the distribution of hair. Do you attach any significance to that, Miss Anderson?

Miss Anderson: There would not necessarily be any alterations as a result of the chromophobe adenoma. A functioning tumor of the pituitary gland such as an eosinophilic adenoma could cause hirsuitism. She had no loss of hair which would be associated with hypo-adrenalism, but that could have occurred later from the pressure of the chromophobe adenoma of the pituitary.

Dr. Delp: Assuming that the calcium value of 2.7 mEq and the phosphorus value of 5.2 mEq are correct, how do you explain them, Mr. Cox?

Mr. Cox: I assume that they are incorrect. If this is a true calcium value, there probably would have been some evidence of tetany, but there was none. Levels of calcium content below 3.75 mEq usually lead to tetany. In my opinion these values are completely reversed, and, if this is the case, both of the levels are in the normal range as would be expected in this case.

Dr. Delp: Miss Anderson, do you believe that the phosphorus level is compatible with the diagnosis?

Miss Anderson: Although the phosphorus value goes up in eosinophilic granulomas, occasionally there is an associated hyperparathyroidism in which the phosphorus is low.

Dr. Delp: Mr. Carper?

Mr. Carper: There is no evidence of control of the parathyroid glands by the pituitary, so the lesion could not have been caused by the lack of pituitary function.

Dr. Delp: What do you believe was the cause of the patient's death, Mr. Cox?

Mr. Cox: Thrombosis, either primary or secondary to spasm, could have led to increased edema and progression of the other signs and symptoms. I also believe that she had an infarct on that side.

Dr. Delp: Do you agree, Mr. Carper?

Mr. Carper: I believe that a thrombus was present. One would not, however, expect to see atherosclerosis in a patient of that age, so the cause of the thrombus is an interesting question. I believe the history of migraine and spasm is significant.

Dr. Delp: Mr. Curran?

Mr. Curran: Progressive massive edema was probably developing on the right side and involving the left side during the first eight or ten hours while her sensorium was still fairly clear. I believe that there was brain stem involvement with pressure against the tentorium and respiratory arrest.

Dr. Delp: Assuming that this was spasm, what is your explanation for it other than the migraine, Mr. Cheatham?

Mr. Cheatham: Blood in the subarachnoid space or the touching or manipulation of any of these vessels could cause spasm which could be transient or could lead to frank infarction of the brain.

Dr. Delp: Dr. Bolinger, what is your explanation for these disturbing calcium and phosphorus values?

Dr. Robert Bolinger (internist): I believe that an error may have been made somewhere.

Dr. Delp: Is it true that the phosphorus is sometimes elevated?

Dr. Bolinger: The phosphorus is frequently elevated in eosinophilic adenoma but not in eosinophilic granuloma of the pituitary. The fact that the calcium is usually not altered is difficult to explain. If the calcium were altered tetany would be present.

Dr. Delp: Do you believe that the patient had acromegaly?

Dr. Bolinger: She was specifically asked questions concerning the signs of early acromegaly. Apparently she had been lactating intermittently. She stated that her shoes had gone up two sizes, and her glove size had increased. Those signs were interpreted as indicating acromegaly. The lactation and amenorrhea could be explained on the basis of a hypothalamic disturbance, but that would not explain the changes in her hands and feet.

Dr. Delp: May we have your comments, Dr. Williamson?

Dr. William P. Williamson (surgeon): Pre-operatively there was little doubt that the patient had a pituitary tumor because of the failure of vision with bi-temporal field cuts. It was my opinion that she had early optic atrophy. She did not appear to be acromegalic. We believed that she had a chromophobe adenoma. The peculiar history of unusually severe migraine headaches with the scotomas was of interest. An arteriogram was done pre-operatively for two reasons: first, to verify the presence of a mass extending from the sella turcica; and, secondly, to determine whether there was a temporal lobe tumor. The arteriogram showed no shift or disturbance of the middle cerebral artery, so it was assumed that that ruled out temporal lobe tumor and intracranial aneurysms and verified supracellar tumor. Without any unusual concern about the risk we proceeded with the craniotomy. The tumor proved to be cystic which accounted for the sudden loss of vision. There was a cyst in the tumor and a hemorrhage in the cyst. On exposure of the tumor the chiasm was markedly compressed, and the optic nerves were stretched around it. The cyst was bluish and fluctuant. A needle was placed in the tumor, and fluid old blood was aspirated, verifying an old sudden hemorrhage which caused the sudden loss of vision. By simple aspiration the tumor was totally collapsed which relieved the chiasm of all of its compression. The reason for the operation was to save her vision. There was no trauma to the carotid artery, and there was no prolonged traction or difficulty with hemostasis. The capsule was opened and inspected down into the sella turcica which was essentially empty. The tumor was mostly cystic, and it was difficult to find enough tumor to obtain a good biopsy specimen. It is significant that, mechanically, there was no trauma or touching of the carotid arteries. The operation proceeded smoothly and easily.

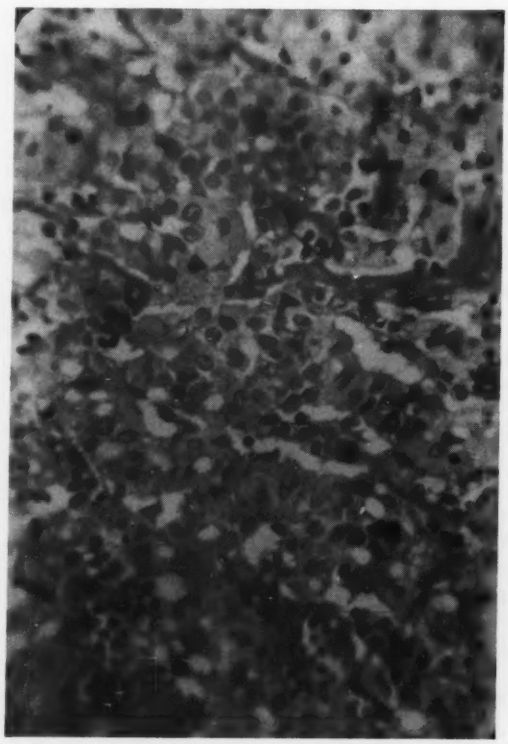

Figure 3. Characteristic chromophobe cells in the pituitary tumor. H. and E.

We were, therefore, shocked and surprised when profound left hemiplegia developed after the operation. The neurosurgeon's immediate problem was whether there was bleeding intracranially from a subdural or extradural hemorrhage. During the first few hours there was hope that the hemiparesis would clear simply as the patient came out of the anesthesia. A spinal tap was done, and her pressure was only 300 mm. with the expected amount of blood which did not appear to be massive intracranial bleeding.

A carotid arteriogram was interpreted as profound spasm of the vessels. The artery tapered off to a small, thin thread and stopped. With the needle in the carotid artery intra-arterial papaverine was injected, but without results. She was given carbon dioxide and oxygen, and the stellate ganglion was blocked, but none of these procedures were effective; the neurological picture did not change. When her pupils became fixed and dilated it was obvious that she was going to die with infarction of the brain and compression of the brain stem.

As a heroic gesture she was returned to surgery for a right frontal lobectomy which can be done without increasing neurological deficit. On opening the dura it was remarkable to see that the arteries of the brain had no blood in them whatsoever; they were completely empty. The veins were black, and the right hemisphere had obviously been infarcted. Knowing that she was going to die the frontal lobe was cut off, and the wound was closed. An interesting observation here is that the patient had had serious severe migraine headaches until she developed a pituitary tumor, whereupon the migraine headaches stopped. As soon as the surgeons touched the pituitary tumor, her arteries went into spasm so severe that they became thrombosed and the patient died.

At that time we had no explanation for that phenomenon, and unless one is forthcoming now, we still have none. I have never seen such an exceedingly rare complication of surgery in the region of the pituitary, and I have never read about it in the experience of anyone else. Many more traumatic operations for craniopharyngeomas and for aneurysms around the Circle of Willis have been performed without causing vasospasm leading to thrombosis.

Dr. Delp: Thank you, Dr. Williamson. May we have your comments now, Dr. Hudson?

Dr. Hudson: This is one of the most intriguing histories that I have ever heard. The extravasation of blood into the subarachnoid is an inconstant cause of vasospasm, and cannot be pinned down definitely to specific situations such as this. Whether or not chemicals can cause vasospasm of such a degree is unknown, but recent observations show that many migraine patients gain 10 to 20 pounds of fluid just before the onset of their headaches, and that, in turn, could explain some of the patient's difficulty with her gloves and shoes. More important from that standpoint, however, is that the fluid accumulation is often primarily localized in the peri-orbital region. Studies of the fluid show that, chemically, it has the characteristics of a polypeptide. When injected into the skin it produces the typical histamine type of response. If a sufficient amount of it is given subcutaneously, even in a normal individual, it will produce shock or lowered blood pressure, all of which has led to the belief that the chemical resembles the old peptone type of antiphylactic substance. An interesting conjecture is that the fluid in the pituitary cyst might have been extravasated (as would normally occur as it was needled), and might have tipped off severe vasospasm in an individual who had inherited tendencies to cerebral vasospasm, as I believe that our patient did.

Dr. Delp: Thank you. May we have your report now, please, Dr. Smith?

Pathological Report

Dr. O. Dale Smith (pathologist):* The patient was a well nourished woman who weighed 160 pounds and was 5 feet and 6 inches tall. She had normal axillary and pubic hair. The surgical defects previously mentioned were present. There was some peri-orbital edema on the right side, and there was some injection of the scleral vessels on the right. The heart, kidneys and liver were not noteworthy. There were few focal areas of atelectasis and some compensatory emphysema in the lung, but these were of minor importance.

The most important changes were in the hypophysis. The posterior lobe was not identified, either grossly or microscopically, and the pituitary was converted into a thin cystic structure about 3 cm. in diameter which filled the expanded sella.

In the normal pituitary a horizontal section clearly shows a tendency for the acidiphils to form in the lateral portions of the anterior lobe, and the basophiles tended to form a mantle around the periphery of the acidophiles. These features were well seen in material stained with periodic acid Schiff and orange dyes which clearly delineated these cell types.

The pituitary tumor when stained by the PAS method failed to show any of its cells which accept these differentiating dyes, and it was then quite characteristic of a chromophobe adenoma (Figure 3). Many areas of the pituitary showed, in addition to hemorrhage and gelfoam, tissue which was cytologically differentiated into the usual acidophiles and basophiles.

* Although a pathologist at the University of Kansas Medical Center at the time of this conference in April, 1959, he is, at the present time, pathologist at the Baptist Memorial Hospital, Kansas City, Missouri.

A survey of the target organs of the pituitary is of interest. The ovaries were symmetric, decreased in size, and had many follicular cysts. They were lined by granulosa, theca interna, and theca externa blending into ovarian stroma. There were no corpora lutea, and there were only a few corpora albicantia. There was no evidence that the patient had ovulated recently or in the distant past. These ovarian changes should not be confused with the polycystic ovaries of Stein-Levinthal which are large. The endometrium was atrophic correlating well with the amenorrhea which she had had for four years. It seems reasonable to conclude that these findings would implicate a failure of the gonadotropins.

There was an overall increase in fibrous tissue and in the production of distinct lobulation. The stroma contained focal collections of lymphocytes which produced lymphoid follicles. The thyroid acini were fairly well filled with colloid, and it must be concluded that this was probably a fairly well-functioning gland. Apparently it had in the past experienced some hyperplasia with irregular involution.

The adrenals appeared normal. Fat stains showed the zona glomerulosa, an area not stimulated by the adenohypophysis, to be depleted of fat. The zona fasciculata and the zona reticularis seemed to be normal. It is interesting to speculate that the hypophyseal changes lead to failure of gonadotropic but not thyrotropic or adrenotropic hormones.

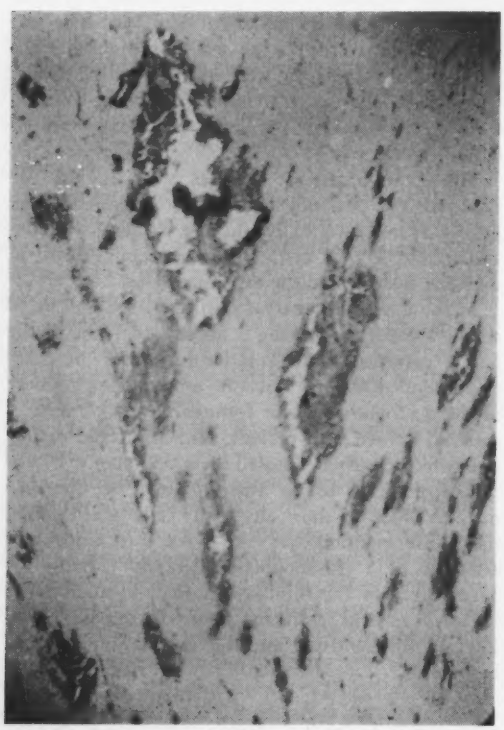

Figure 4. Recent infarction of nervous tissue, petechial hemorrhage and vascular congestion in the right cerebral hemisphere.

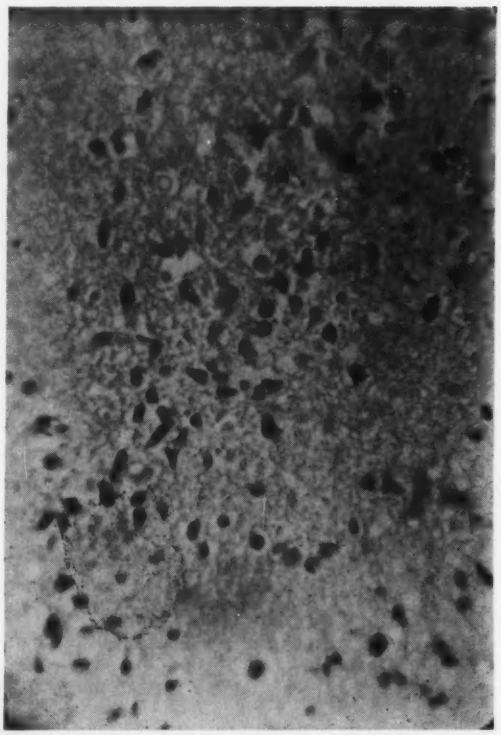

Figure 5. Marked chromatolysis and pyknosis of neurons in Ammon's Horn in right cerebral hemisphere.

The lumen of the right internal carotid artery was filled with fibrin, red cells and masses of platelets. There was some early reaction in the vessel wall which showed changes of recent thrombosis. The right cerebrum showed the diffuse changes which occurred with the occlusion of the right internal carotid artery. The entire right cerebral hemisphere was infarcted *(Figure 4)* which probably accounted for her terminal event.

The neurons in Ammon's Horn on the right *(Figure 5)* showed marked chromotolysis and pyknosis, but because the nuclei were still present we must accept this as being recent. There was no evidence of gliosis or fibrosis. A comparable area from the Hippocampus on the left was normal *(Figure 6)*.

Dr. Delp: Are there any questions of Dr. Smith?

Mr. Curran: To what part of the internal carotid were you referring?

Dr. Smith: It was intracranially as it exists from the base of the skull.

Dr. Hudson: Assuming that there was no thrombus at the end of surgery, how long do you believe

it would have taken for occlusion to occur from thrombus formation?

Dr. Smith: Neutrophiles were beginning to accumulate around the vessel, and I would judge that it would take several hours after the initial thrombosis.

Dr. Delp: The patient lived for 24 hours after surgery, and that is a long time.

Dr. Hudson: She was immediately hemiplegic. She responded within an hour from the time the wound was closed, and the hemiplegia was profound at that time.

Dr. Smith: I believe the changes in the vessels were compatible with thrombosis within the 24 hours.

Dr. Delp: Dr. Steegmann, you saw the patient in 1952 and subsequently in consultation; may we have your comments about her migraine?

Dr. A. T. Steegmann (neurologist): There was no question in my mind that she had migraine. The old x-rays showed the sella to be completely normal. There was a family history of migraine, and, apparently, her second disease was acquired later.

Dr. Delp: This patient had the most classical history of migraine I have ever heard or seen. She had absolutely every manifestation, but the headaches stopped at about the time the pituitary tumor developed. I do not know whether that is a suggestion or a clue as to the etiology of migraine.

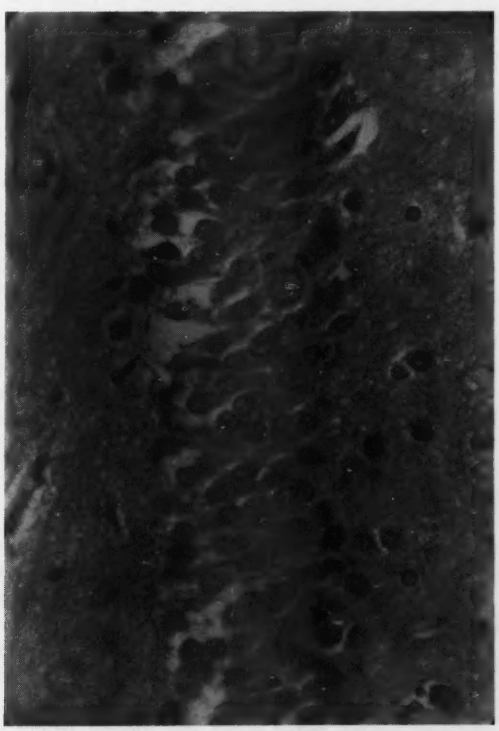

Figure 6. Ammon's Horn in left cerebral hemisphere showing normal neurons.

The phosphorus values were stressed here because, as many of you know, the laboratory manifestation of excess growth hormone is an elevated serum organic phosphorus. Unfortunately, I am sure that this is only a reversal in recording calcium and phosphorus levels on the patient's chart.

Pathological Anatomical Diagnosis

Chromophobe adenoma of the pituitary, 3 cm.

Pressure atrophy of remaining pituitary.

Atrophy of the ovaries, and the endometrium, moderate.

Recent thrombosis of the right middle cerebral artery, advanced.

Recent infarction of the right frontal, parietal and temporal lobes of the brain and of the left basal ganglia.

Tracheotomy

(Continued from page 395)

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Gullibility is the key to all adventures. The greenhorn is the ultimate victor in everything; it is he that gets the most out of life.—*G. K. Chesterton*

What is now proved was once only imagined.

Studies on the Effect of Tetanus Antitoxin Against Tetanus Toxin

HOWARD CHIN, M.D., ***Oakland, California***

TETANUS IS A DISEASE of man and animals characterized by spasms of voluntary muscles. The spasms are often most marked in the muscles of the neck, jaw, hence the name "lockjaw." The disease is caused by the very potent toxin produced by *Clostridium tetani*. The tetanus bacillus was first described in 1884 by Nicolaier. Kitasato, in 1889 isolated the organism in pure culture and demonstrated its casual significance. According to the experimental evidence of Meyer and Ransom, the toxin is absorbed by the end plates of the motor nerves and travels to the ganglion cells of the central nervous system along the axis cylinders of the peripheral nerves. Liquid cultures are highly toxic; 5 x 10 cubic centimeter of liquid culture may be fatal to a mouse weighing 10 grams. Hall repeatedly produced toxin of which the minimum lethal dose for a guinea pig was rarely more than 0.0001 cubic centimeter.

Passive immunization of man with tetanus antitoxin, produced in horses, provides circulating antibody which combines with toxin and renders it harmless. But once symptoms of tetanus have appeared, resulting from tetanus toxin absorbed by the motor end plates, tetanus antitoxin can not dislodge it. The affinity of the nervous tissue, for tetanus toxin is very great, and symptoms of tetanus may appear in spite of the presence of circulating antibody. Prevention of tetanus from injuries could be accomplished by debridement and the administration of antibiotics, notably penicillin and tetracylines, within 24 hours after inoculation of tetanus spores. Turner found that after administering a therapeutic dose of tetanus antitoxin in patients, the protective level of tetanus antitoxin against tetanus toxin lasted at least seven days. The importance of maintaining a certain level of serum tetanus antitoxin in rabbits to prevent death from tetanus was described by Prodovsky and Turner. A fatal case of tetanus was reported by Littlewood and Mant in 1954 despite the fact that the patient had received the accepted prophylactic dose of tetanus antitoxin. History in this patient revealed that he had also been given a prophylactic dose of tetanus antitoxin after an injury 6 months previously. The authors postulated that if a patient is sensitized against horse serum, the second or subsequent injection of tetanus antitoxin, equine origin, led to an accelerated removal from the blood.

Presentation of Problem

The present paper describes experiments to determine: a) The 50 per cent lethal dose of tetanus toxin for mice. b) The minimum amount of tetanus antitoxin needed to protect these mice against at least one LD_{50} of tetanus toxin. c) The duration of protection of tetanus antitoxin in mice. d) To see if mice that have been injected with antitoxin contained within a foreign protein, horse serum, will develop antibody against horse serum and thereby render a subsequent injection of antitoxin less effective against tetanus toxin.

This is one of a group of theses written by fourth year students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be best by the faculty at the school. Dr. Chin is now at the Children's Hospital of the East Bay, Oakland, California.

Methods and Results

Experiment 1. DETERMINATION OF THE POTENCY OF TETANUS TOXIN IN MICE:

Tetanus toxin was diluted as follows: 1:1000, 1:2000, 1:5000, 1:10,000, 1:20,000, 1:40,000, 1:60,000, 1:80,000, 1:100,000 and 1:1,000,000. One tenth milliliter of each dilution was then injected intramuscularly into the left thigh of 2 Hauschka strain mice, 6 weeks old, weighing between 25-30 grams.

The LD_{50} was approximately one tenth milliliter of 1:20,000 dilution of stock toxin. Mice injected with a lower dilution all died within 5 days, while those with a higher dilution all showed signs of paralysis at the site of injection, but none died. These recovered completely from their paralysis within 60 days.

Experiment 2. DETERMINATION OF THE PROTECTIVE VALUE OF TETANUS ANTITOXIN AGAINST TETANUS TOXIN:

Tetanus antitoxin, equine origin (obtained from the National Drug Company, stock number 78085 contained 1000 units per milliliter), was diluted so that each tenth of a milliliter contained 1 unit of tetanus antitoxin. Three groups of 8 mice each were given the following amount of tetanus toxin: Group I was injected intramuscularly into left thigh with 0.1 cc. of 1:2000 tetanus toxin (approximately 10 LD_{50}). Group II was injected intramuscularly with 0.1 cc. of 1:1000 tetanus toxin (approximately 20 LD_{50}). Group III was injected intramuscularly with 0.1 cc. of 1:500 tetanus toxin (approximately 40 LD_{50}). Then 2 mice from each group of 8 were injected intramuscularly into right thigh with either 0.2 cc. physiologic saline, 1 unit, 2 units or 4 units of tetanus antitoxin. The interval between the administration of the tetanus toxin and antitoxin was less than 30 minutes.

One to 4 units of tetanus antitoxin protect mice against death after injection of up to 20 LD_{50} of tetanus *(table 1)*. With similar amount of tetanus

Table 1

TETANUS TOXIN - ANTITOXIN TITRATION
HAUSCHKA MICE
6 WKS. OLD, 25-30 GMS.

UNITS OF TETANUS ANTITOXIN	TETANUS TOXIN (0.1 cc. I.M.)					
	10 LD_{50} GROUP I		20 LD_{50} GROUP II		40 LD_{50} GROUP III	
0	18	18	18	65	18	18
1	65		40		240	72
2			18		18	72
4					240	72

NUMBERS IN SQUARES INDICATE TIME OF DEATH IN HOURS

NUMBER IN LOWER LEFT CORNER INDICATE ONSET OF PARALYSIS OF LEFT HIND LEG IN HOURS

antitoxin, there is partial protection against 40 LD_{50} of tetanus toxin. In Group I, injected with 10 LD_{50} of tetanus toxin, only one mouse showed signs of left leg paralysis, after having received 1 unit of tetanus antitoxin previously. Other mice, having received a greater amount of tetanus antitoxin (2 and 4 units), showed no signs of paralysis. In Group II, injected with 20 LD_{50} of tetanus toxin, one mouse after having received 1 unit of tetanus antitoxin and 1 mouse after having received 2 units of tetanus antitoxin, showed signs of paralysis of left hind leg, the site of tetanus toxin injection, while mice that had received 4 units of tetanus antitoxin showed no signs of paralysis. In group III, injected with 40 LD_{50} of tetanus toxin, all mice showed signs of paralysis, whether they had received 1, 2, or 4 units of tetanus antitoxin. The onset of paralysis showed no correlation with the amount of tetanus antitoxin received. Signs of left leg paralysis began between 18 to 72 hours after the injection with tetanus toxin. All mice had complete recovery from paralysis within 60 days.

Experiment 3. DETERMINATION OF DURATION OF PROTECTION BY TETANUS ANTITOXIN:

Three groups of 28 mice each were used in this experiment to receive either 1, 2, or 4 units of tetanus antitoxin. From each group, 6 mice served as controls. One injection of tetanus antitoxin was given to two mice from each group from the 20th day and every other day up to and including 0 day, at which time 0.1 cc. of 1:1000 tetanus toxin (approximately 20 LD_{50}) was injected intramuscularly into all mice.

The duration of protection by antitoxin against tetanus toxin was about 8 to 10 days *(table 2)*. In a later experiment, this was shown to be approximately 7 days *(table 3b)*. The majority of the animals that had received tetanus antitoxin for 10 to 20 days before the challenging dose no longer had a sufficient antitoxin level to afford protection to a subsequent challenge dose of 20 LD_{50} of tetanus toxin. One animal after having received 1 unit of tetanus antitoxin on the 14th day survived. Three animals after having received 2 units of tetanus antitoxin on the 20th, 14th, and 12th day respectively survived. One animal after having received 4 units of tetanus antitoxin on the 18th day and 2 animals on the 14th day survived, while all animals after having received 4 units of tetanus antitoxin on the 10th day died. These survivals were attributed to biological variation. Such variation may explain death of one animal that had received 1 unit of tetanus antitoxin only 6 days before the challenging dose of tetanus toxin.

Experiment 4. EFFECT OF PRETREATMENT WITH TETANUS ANTITOXIN (HORSE SERUM) ON SUBSEQUENT TETANUS PROPHYLAXIS:

Two groups of mice were used in this experiment: The first group of mice was subdivided into 3 subgroups: a) One subgroup of 14 mice was injected intramuscularly with 1 unit of antitoxin. b) A second subgroup of 14 mice was injected with 2 units of antitoxin, and c) The third subgroup of 14 mice was injected with 4 units of antitoxin. Additional 10 mice were used as control for the pretreated group. These pretreated mice were left in their cages for 18 days. Then on the 18th day, and every other day thereafter including day 0, 2 mice from each subgroup of the pretreated and non-pretreated groups a), b) and c) were given an injection of 1, 2, and 4 units of antitoxin. The second group of mice was not pre-injected with tetanus antitoxin before the 12th day. They received only one injection of tetanus antitoxin starting from the 12th day to day 0. On day 0 both groups, the pretreated and the non-pretreated groups were injected with 20 LD_{50} of tetanus toxin intramuscularly.

Comparison of protection afforded by tetanus antitoxin in mice once pretreated or not, showed little difference, either in mortality of paralysis *(table 3a and 3b)*. The median time of death in the pretreated group was 6.0 days, while in the non-pretreated group, it was 7.3 days. Even 4 units of antitoxin injected in a single dose failed to produce a sufficient amount of antibody against horse serum.

Experiment 5. EFFECT OF PRETREATMENT WITH TWO DOSES OF TETANUS ANTITOXIN (HORSE SERUM) 30 DAYS APART ON SUBSEQUENT TETANUS PROPHYLAXIS:

Two groups of mice were used in this experiment: The first group of mice was subdivided into 3 subgroups injected with 1, 2, or 4 units of tetanus antitoxin on 67 and 37 days prior to day 0. The second group of mice was not pretreated with tetanus antitoxin before the 7th day. Then from the 67th (–7 day), 66th (–6 day), 65th (–5 day), 64th (–4 day) and 0 day, 2 mice from each subgroup, of the pretreated and the non-pretreated groups, were given injections of 1, 2, and 4 units of tetanus antitoxin. As for control for persistence of passive immunity, 10 mice given 4 units of tetanus antitoxin on –67th and –37th day were used.

On 0 day, all mice were injected with a dose of tetanus toxin 20 times LD_{50} intramuscularly.

The data in table 4 indicate that when mice were preinjected with 2 doses of tetanus antitoxin (horse serum) 30 days apart, they were no longer protected by tetanus antitoxin given 4 to 7 days previously. It may be postulated that these mice had developed sufficient amount of antibody against horse serum to interfere with the protective value of tetanus antitoxin against tetanus toxin. When comparing data with table 3 and 4, it appears that the second booster dose of tetanus antitoxin had increased the level of antibody against horse serum to a significant level, so that a subsequent protective dose of tetanus anti-

DURATION OF PROTECTION BY TETANUS ANTITOXIN

Table 2

HAUSCHKA MICE
6 WKS. OLD, 25-30 GMS.
TETANUS - ANTITOXIN

DAYS	1 UNIT	2 UNITS	4 UNITS
−20	fighting 40h / 20h	50h / 40h 4d	24h 24h / 20h 20h
−18	40h 40h / 20h	30h 40h / 20h 20h	24h /
−16	30h 20h / 20h 20h	fighting 24h /	24h 30h / 20h 24h
−14	5d / 20h	40h / 20h 40h	/
−12	24h 30h / 20h	30h / 20h 6d	26h 30h / 20h
−10	/	40h 6d	50h 65h / 20h 24h
− 8	/	/	40h /
− 6	6d / 40h	65h 4d	40h /
− 4	6d /	/	/
− 2	/	/	/
20 LD_{50} TETANUS TOXIN GIVEN 0	26h /	/	4d /
+ 1	22h 26h / 20h 20h	26h 26h / 20h 20h	22h 26h / 20h 20h
+ 2	24h 26h / 20h 20h	24h 24h / 20h	24h 30h / 20h 20h
+ 3	24h 30h / 20h 20h	24h 30h / 20h 20h	24h 30h / 20h 20h

LEGEND: RF LF / RH LH = PARALYSIS OF CORRESPONDING LEG; ■ = DEATH; h = HOURS; d = DAYS

NUMBERS NEXT TO SQUARE INDICATE TIME OF ONSET OF PARALYSIS OR DEATH

MICE RECEIVED 1 DOSE TETANUS ANTITOXIN PREVIOUSLY

Table 3a NUMBERS IN SQUARES INDICATE TIME OF ONSET OF PARALYSIS IN HOURS

HAUSCHKA MICE, 6 WKS. OLD, 25-30 GMS.

DAYS	PRE-TREATED WITH 1, 2, & 4 UNITS OF ANTITOXIN 18 DAYS BEFORE -12th DAY						NOT PRE-TREATED MICE					
	1 UNIT		2 UNITS		4 UNITS		1 UNIT		2 UNITS		4 UNITS	
-12	20	20	20	20	20	20	20	20	20	20	20	40
-10	20	20	20	20	20	20	20	20	20	20	20	58
- 8	20	20	20	20	20	20	20	20	20	20	20	20
- 6	58	20	20	20		20	20	20	20	20	20	20
- 4	20		20						20			
- 2												
* 0	24	24	24		24		58	58			65	
CONTROL	20	20	20	20	20	20	20	20	20	20	20	20
	20	20	20	20			20	20	20	20		

TETANUS ANTITOXIN GIVEN 4 HRS. BEFORE TETANUS TOXIN

RECEIVED 4 UNITS OF TETANUS ANTITOXIN 30 DAYS BEFORE 0 DAY

CONTROLS RECEIVED NO TETANUS ANTITOXIN

* AT 0 DAY ALL MICE WERE GIVEN 20 LD_{50} TETANUS TOXIN

Table 3b NUMBERS IN SQUARES INDICATE TIME OF DEATH IN HOURS

DAYS	PRE-TREATED MICE							NOT PRE-TREATED MICE						
	1 UNIT		2 UNITS		4 UNITS		MEAN TIME OF DEATH	1 UNIT		2 UNITS		4 UNITS		MEAN TIME OF DEATH
-12	24	24	24	58	30	40	33	24	30	40	72	30		39
-10	30	72	40	65	75		56	58	58	24	75	72		58
- 8	30	58	30	75	40	24	43	24	72			136		78
- 6		58	24	24			35	72	82	108	120			98
- 4	136													
- 2														
* 0														
CONTROL	24	24	24	24	24	24		20	20	20	20	24	24	
	24	24	24	36				24	24	24	24			

RECEIVED 4 UNITS OF TETANUS ANTITOXIN 30 DAYS BEFORE 0 DAY

CONTROLS RECEIVED NO TETANUS ANTITOXIN

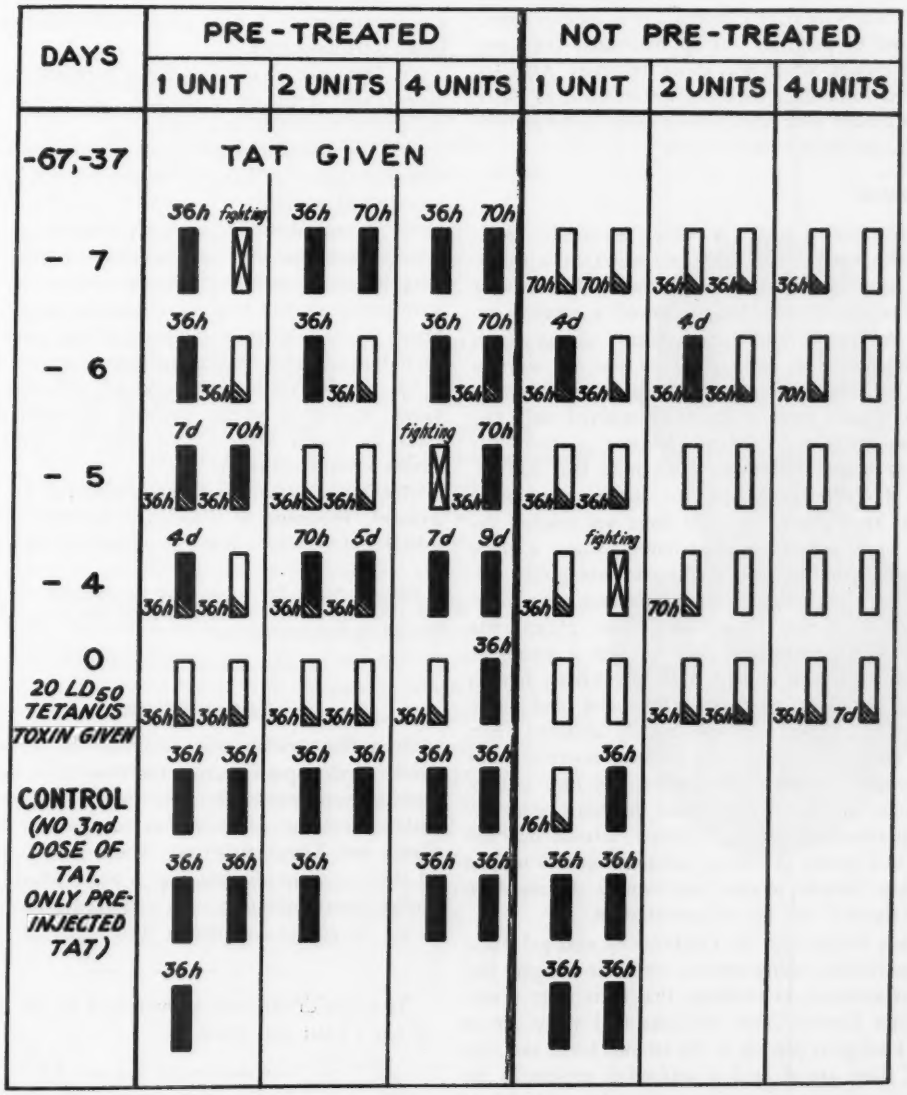
MEDIAN TIME OF DEATH = 6 DAYS

MEDIAN TIME OF DEATH = 7.3 DAYS

MICE RECEIVED 2 DOSES TETANUS ANTITOXIN 30 DAYS APART

Table 4

HAUSCHKA MICE
6 WKS. OLD, 25-30 GMS.



LEGEND: ▯ = PARALYSIS ▮ = DEATH h = HOURS d = DAYS

NOTE: THESE MICE WERE CHECKED EVERY 12 HRS. NUMBERS NEXT TO SQUARES INDICATE TIME OF ONSET OF PARALYSIS OR DEATH

toxin no longer afforded protection against a challenging dose of 20 LD_{50} tetanus toxin. This was clearly shown in table 4, when the pretreated and non-pretreated groups of mice were compared. In the pretreated group of 30 mice, there were a total of 18 deaths due to tetanus toxin. In the non-pretreated group, there were only 2 deaths due to tetanus toxin. The onset of paralysis was approximately the same in both groups, which was about 36 hours. All mice recovered from their paralysis within 60 days. Mice in both groups died from tetanus from 36 hours to 9 days, the majority within 3 days.

Discussion

Kind reported that in mice previously sensitized with horse serum with one injection, a subsequent injection of tetanus antitoxin, after having been challenged with toxin, showed a marked decrease in prophylactic effectiveness against death from tetanus. The data *(table 3)* did not show a significant difference in prophylactic effectiveness against tetanus in mice that had received only one previous injection of tetanus antitoxin, which was horse in origin. However, when mice that had received 2 doses of horse serum (tetanus antitoxin) 30 days apart *(table 4)*, then there was marked decrease in prophylactic effectiveness, when a third protecting dose of tetanus antitoxin was given, followed by a challenging dose of tetanus toxin. Tetanus antitoxin was chosen instead of plain horse serum for the sensitizing doses because it would be more analogous to clinical medicine, where, besides tetanus antitoxin, pertussis, diphtheria and other antitoxins are used and are usually obtained from horse serum. A combination of these injections may be enough to sensitize the person and may account for some of the anaphylactoid reactions after receiving tetanus antitoxin. Likewise, tetanus may develop in a person in spite of adequate dose of tetanus antitoxin because tetanus antitoxin is destroyed in an accelerated rate due to sensitization.

It was found with the Ouchterlony agar-gel diffusion technique, using tetanus toxin as antigen and tetanus antitoxin as antibody, that there were 4 visible lines formed. This indicates that there are at least 4 antigens present in the tetanus toxin and similarly, there are at least 4 antibodies present in the tetanus antitoxin of equine origin. It would be of interest to purify the tetanus toxin and see which one or more of the antigens would produce tetanus. And if a pure fraction of the tetanus antitoxin which contains the antibody against tetanus could be obtained, possibly by the electrophoretic method, then we may be able to use this fraction in an emergency situation to treat patients who are sensitive to horse serum, and an anaphylactoid reaction might be avoided, since only a very small amount would be used. An alternative method would be the use of hyperimmune human gamma globulin. Thorough debridement with chemotherapy, in any event, would still be required.

Summary

1). The LD_{50} of tetanus toxin in Hauschka mice was approximately 0.1 cc. of 1:20,000 dilution, injected intramuscularly.

2). One unit of equine tetanus antitoxin protects mice against death up to 20 LD_{50} of tetanus toxin and partial protection up to 40 LD_{50}.

3). The duration of protection afforded by tetanus antitoxin against 20 LD_{50} of tetanus toxin is approximately 7 days in mice.

4). In mice that had previously received one dose, a subsequent dose of tetanus antitoxin did not show a significant decrease in effectiveness. However, when mice previously had received 2 doses of tetanus antitoxin, 30 days apart, a subsequent dose gave little protection against a challenging dose of tetanus toxin.

5). By the Ouchterlony agar-gel diffusion technique, at least 4 antigen-antibody precipitin bands could be shown when tetanus toxin was used with equine tetanus antitoxin.

Acknowledgment: I am very grateful to Dr. J. K. Frenkel, Professor of Pathology, KUMC, for his advice and assistance in the preparation of this paper.

Editor's Note: References may be obtained by writing the JOURNAL OF THE KANSAS MEDICAL SOCIETY, 315 West 4th Street, Topeka, Kansas.

Superstitions

Even the time-honored ceremony of breaking a bottle of champagne across the bow of a ship has roots in superstition. It dates from the days when sailors went out of their way to appease the sea. Greek and Roman fishermen would leave a portion of their catch on the beach as a peace offering, and Indo-Chinese fishermen once sacrificed a man yearly to the sea god as the price of their fleet's safe return.

True wealth can only be measured by the richness of one's heart and mind.

Once you have missed the first buttonhole you'll never manage to button up.—*Goethe*

Loyalty cannot be coerced or compelled, it has to be won.—*A. Whitney Griswold*

A thick skin is a gift from God.

—*Konrad Adenauer*

The President's Message

DEAR DOCTOR:

I wish I might report an improvement in my health so I could personally attend to the obligations you entrusted into my care. There is an indescribable urgency within me to aid in solving the many problems confronting the practice of medicine. I long for the day when this dream may be a reality. I have not given up hope.

Meanwhile many have taken over my duties in your behalf and Society activities are being accomplished. To each of you my sincerest gratitude. I follow your successes with great interest.

May I call your attention at this time to several projects I believe are worthy of special mention.

A new Relative Value Scale is now on the presses. This greatly expanded document will reach you in a few days. I envision it to become the basis for the creation of all future fee schedules. Blue Shield hopes to convert existing schedules into this scale by 1963. In your private practice you will find the new Relative Value Scale of interest and perhaps helpful.

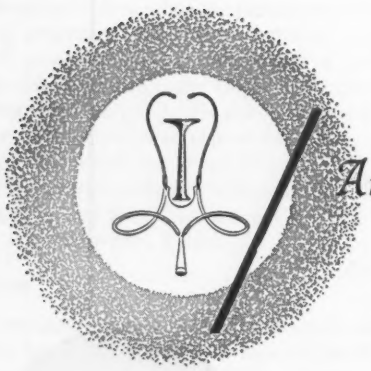
The Public Relations Committee is conducting a one day conference at Emporia on Sunday, September 17, 1961. All members are invited to attend and we especially urge each component society to be represented. The meeting will be of interest to you, but more important, it is designed to coordinate the public relations efforts of the entire state.

There is work being done on safety, welfare programs, on relations with the Bar Association and many other projects. You will hear more about these and of others through the Council. In the meantime, I wish you each every success in your personal and in your society activities toward the end that we may render the people in this state the finest medical care in the world.

Fraternally yours,

Harold M. Glover, M.D.

President



Announcements

Professional meetings, conferences, and postgraduate courses of national importance are listed for the* Doctor's Calendar. *Notice of the session is posted in advance to allow the physician time to make preparations.

The American College of Chest Physicians will hold its annual Interim Session at the Brown Palace Hotel in Denver, Colorado, November 25-26.

The scientific sessions will be held on Saturday morning, November 25, and on Sunday afternoon, the 26th. The Board of Regents and Board of Governors of the College will meet on Saturday afternoon.

Subjects to be discussed will include diagnosis and treatment of congenital and acquired cardiovascular diseases, pulmonary infections, emphysema, and pleural effusions. Other items of interest are diagnosis and treatment of coronary insufficiency, evaluation of drugs for treatment of heart failure, inhalation therapy, bronchitis and bronchial asthma, carcinoma of the lung, chronic cor pulmonale, paroxysmal tachycardia, and diseases of the esophagus.

A speaker from this area will be Antoni M. Diehl, M.D., Kansas City.

A program may be obtained by writing the Executive Offices of the College at 112 East Chestnut Street, Chicago, Illinois.

The 1961 Scientific Session is to be held in conjunction with the American Cancer Society's Annual Meeting, October 23-24, 1961, in New York City, at the Biltmore Hotel.

The topic will be "The Physician and the Total Care of the Cancer Patient."

For further information write to the Professional Education Section, American Cancer Society, 521 West 57th Street, New York 19, New York.

The Arthritis and Rheumatism Foundation offers predoctoral, postdoctoral and senior investigatorship awards in the fundamental sciences related to arthritis for work beginning July 1, 1962. Deadline for applications is October 31, 1961.

These awards are intended as fellowships to advance the training of young men and women of promise for an investigative or teaching career. They are not in the nature of a grant-in-aid in support of a research project.

For further information and application forms, address the Medical Director, Arthritis and Rheumatism Foundation, 10 Columbus Circle, New York 19, New York.

The Council on Scientific Assembly invites physicians to submit titles and brief abstracts of scientific papers they wish to deliver at the 1962 annual meeting of the American Medical Association, which will be held in Chicago, June 11-15. The deadline is October 15.

"We would like to receive as many titles and abstracts as possible," said Council Chairman Samuel P. Newman, of Denver, "because in that way we have better selection and this, in turn, assures a more timely and better scientific program."

Physicians who wish to participate in the Chicago scientific program and desire information are invited to write to Dr. Charles Bramlitt, Secretary, Council on Scientific Assembly, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois, or to any council member.

The 1961 Fall Clinical Conference of the Kansas City Southwest Clinical Society will be held at the Hotel Muehlebach in Kansas City, Missouri, September 18-20, with nineteen distinguished guest speakers from throughout the United States being featured on the program.

(Continued on page 426)

Blue Shield

Optional Benefits

At one time Blue Shield had one standard membership agreement providing a uniform set of benefits for all subscribers. Through the years, various optional programs have been developed in response to requests from subscribers and physicians for more flexible plans.

Optional benefits naturally present many problems of interpretation for both the physician and the subscriber and it is very difficult for anyone to be completely familiar with all aspects of a program. However, the situation may not be as bad as it appears and a brief review of the options available to subscribers may be of some value in understanding the overall Blue Shield programs.

Basic Benefits

The vast majority of subscribers have either Fee Schedule 1 ($3,000 family income) or Fee Schedule 2 ($4,500 family income). These are the standard state-wide programs selected by over 90 per cent of the subscribers. There are other basic schedules, and employees of firms doing business in several states often have a special national program such as the Skelly Oil Company or U. S. Steel Program where the benefits vary from the two standard Schedules 1 and 2.

The most widespread example of a national account is the Federal Employee Program which has a fee schedule with two optional levels of benefits known as High Option or Low Option. Members of the Federal Employee Program are issued special identification cards which makes it relatively easy to recognize such members.

Riders

In addition to basic programs such as Fee Schedule 1 or 2, subscribers in employee groups may select riders that provide services not available in the basic schedules. The most popular is the Diagnostic X-ray Rider which provides for non-accident x-rays. The Rider held by most subscribers provides for diagnostic x-rays either in or out of the hospital according to a Schedule. There are a few X-ray Riders with limitations that are sold only in sharp competitive situations.

Another option is the OUT-PATIENT LABORATORY SERVICES RIDER designed to provide benefits for pathology services. This is available only to groups.

A relatively new and low cost development is the Supplemental Accident Rider which provides additional benefits for professional services required as a result of accidental injury. The group selects one of three levels of benefits: $250, $1,250 or $2,500.

The EXTENDED BENEFITS RIDER is available to groups *or* individuals and covers nine specified illnesses including polio, leukemia and cancer. Over 390,000 members have this program.

Major Medical

Groups may now select a MAJOR MEDICAL Plan. "Basic" benefits such as Schedule 1 or 2 are provided and in addition, services such as home and office calls, laboratory services, prescription drugs, private duty nursing and limited dental services are covered. These added benefits are usually subject to a deductible such as $100, $200 or $300 per year and the Blue Shield payment is then a per cent of the balance, with 80 per cent being the most common figure.

For the most part, the Participating Physicians Manual contains detailed information regarding Schedules 1 and 2 and the Riders. Completely detailed

(Continued on page 426)

From the Stacks

State Medical Library

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Recent Acquisitions

Anatomy
Lockhart, R. D. Anatomy of the human body. Lippincott. 1959.

Bacteriology
Kimler. A. Manual of clinical bacteriology. Lippincott, 1961.

Biochemistry
Luck, J. M. Annual review of biochemistry. Annual Reviews. 1961.
Sunderman, F. W. Lipids and the steroid hormones in clinical medicine. Lippincott. 1960.

Biography
Kobler, J. The reluctant surgeon. Doubleday. 1960.

Cardiovascular System
Edwards, J. E. An atlas of acquired diseases of the heart & great vessels. Volumes 1-3. Saunders. 1961.
Kuhn, R. A. New hope for stroke victims. Appleton-Century-Crofts. 1960.
Moyer, R. F. Cardiovascular dynamics. Saunders. 1961.
Reube, F. C. Essential hypertension. Springer, Verlag. 1960.
Rushmer, R. F. Cardiovascular dynamics. Saunders. 1961.
Taussig, H. B. Congenital malformations of the heart. Harvard Univ. Press. 1960.

Communicable Diseases
Top, F. H. Communicable & infectious diseases. Mosby. 1960.

Would you like to have the librarian research articles for you on a given subject?

Remember, books and periodicals will be sent anywhere in the state. We will bill you, four cents for the first pound and one cent for each additional pound.

Dentistry
Thoma, K. H. Oral & dental diagnosis. Saunders. 1960.

Dermatology
Year Book of dermatology. Saunders. 1961.

Endocrinology
Ciba Foundation. Metabolic effects of adrenal hormones. Little, Brown. 1961.
Ibid. Adrenergic mechanisms. Little, Brown. 1960.
Harrison, R. G. The adrenal circulation. C. C Thomas. 1960.

Gastroenterology
Kennedy, R. H. Nonpenetrating injuries to the abdomen. C. C Thomas. 1960.

History
Hashinger, E., and Arthur E. Hertzler: The Kansas horse & buggy doctor. University of Kansas Press. 1961.

Hypnosis
Meares, A. A system of medical hypnosis. Saunders. 1961.

Medical Profession
Medical Exam. Pub. Co. Medical. Exam Review Book 7. Internal Medicine. 1961.
Miller, G. Teaching & learning in medical school. Harvard Univ. Press. 1961.

Medicine
Nagan, P. S. Medical almanac. Saunders. 1961.

Mental Health
Ridenour, N. Mental health in the U. S. Harvard Univ. Press. 1961.

Mortuary Science
Gale, F. Mortuary science. C. C Thomas. 1961.

Musculoskeletal System
Hollingshead, W. H. Functional anatomy of limbs & back. Saunders. 1960.

Nervous System Diseases
Cooper, I. S. Parkinsonism. C. C Thomas. 1961.
Swank, R. L. A biochemical basis of multiple sclerosis. C. C Thomas. 1961.

Nursing
Sister Mary Bernadette. Life of a student nurse. Myers. 1961.

Nutrition
Gordon, R. Therapeutic meal plans. Univ. of Kansas Press. 1960.

(Continued on page 426)

Book REVIEWS

MEDICAL ALMANAC—1961-62. Compiled by Peter S. Nagan, and published by W. B. Saunders Company.

This is the first edition of what the author hopes may become a regularly revised reference book. It is like other almanacs—there is a tremendous amount of data included within its 500 plus pages. It should be useful as a reference book for editors, librarians, government officials, writers, etc., and in addition it is interesting to pick it up, let it open anywhere, and start reading. You may not find use for the information you read, but the chances are good that you will enjoy your browsing through the book. Included are descriptions of all the certification boards, statistics about hospitals, hospital and medical costs, a listing of national organizations and their meetings, a tabulation of all the medical schools in the country, research projects and grants, income tax information, Selective Service regulations, a listing of Nobel prize winners, etc., etc. Not a book to read from cover to cover, not one to which you will refer daily or from which you will get any clinical helps, it is still interesting reading and a useful source of statistical information.—*O.R.C.*

A SYNOPSIS OF PHYSIOLOGY—by C. C. N. Vass, pp. 348, Williams and Wilkins, Baltimore, Ed. 5, 1961.

Probably all of us, when we think of a medical physiology book, visualize a tome of imposing proportions packed with so much discussion of experimental procedures that the conclusions—the facts—are all but inaccessible. This synopsis is the reverse.

In a volume that is almost small enough to put into one's jacket pocket the author has packed the facts of human physiology stripped of all but the barest explanations. The synopsis is not intended to replace standard textbooks or references, but rather to supplement them by presenting a rather complete summary for quick factual reference or review. It makes it possible for the student or physician to renew and extend his knowledge in a minimum amount of time.

Material is presented in outline form with an abundance of figures and tables. This makes it possible to present an enormous amount of factual material in a book of really small size. The printing and binding are good, and the index appears to be adequate.—*J.D.R.*

THE CARDIAC ARRHYTHMIAS. Brendan Phibbs, M.D. C. V. Mosby Company, 1961.

This book is intended to teach physicians who are not cardiologists to diagnose and treat cardiac arrhythmias. As the author states, almost all physicians need to be competent in the diagnosis and treatment of cardiac arrhythmias. Frequently, critical decisions must be made in a matter of minutes and time is not available for consultation. This book is a concise summary on the diagnosis and treatment of cardiac arrhythmias. The average physician can read it through and assimilate its contents in one or two evenings. The text is amply supplemented with numerous representative electrocardiographic tracings illustrating the various arrhythmias. Diagrams showing the abnormal mechanisms involved in the arrhythmias will be found very helpful to those physicians who have had little experience with the electrocardiogram. Explanations are clear and concise. The author has done an excellent job in presenting a complicated subject in a concise clear form. Although the experienced cardiologist may find this book too elementary for him, the physician without special training in cardiology and electrocardiography will welcome the simple easy-to-understand presentation of the arrhythmias that Doctor Phibbs presents in this book.

The book is divided into five sections. The first two on Anatomy and Physiology and Electrical Registration of the Heartbeat comprise only a few pages. The third section, Abnormal Mechanisms as Registered in the Electrocardiogram makes up 90 per cent of the book. This section also includes a chapter on cardiac arrest during surgery. Part four is a brief section on clinical diagnosis of cardiac arrhythmias. Throughout the book the author repeated-

(Continued on page 426)

Editorial COMMENT

Industrial Schools

(The Division of Institutional Management of the State Board of Social Welfare prepared a statement of the functions and admission procedures of the eleven state institutions under its direction. This information will be published serially during the next several months.—Ed.)

The Industrial School for Girls is located at Beloit, Kansas, and the Industrial School for Boys at Topeka, Kansas.

Commitment is made under the Juvenile Code by the Juvenile Court. Mentally deficient, psychotic, dependent, or neglected children should not be committed to an Industrial School, but should be referred to other sources designed for their particular problems.

When a child has been adjudged to be a delinquent child, or a miscreant child, under provisions of the Juvenile Code, the judge of the juvenile court may commit such child, if a boy, to the State Industrial School for Boys, or may commit such child, if a girl, to the State Industrial School for Girls.

Delinquent is defined as a boy less than 16 years of age, or a girl less than 18 years of age (other than a "traffic offender") who does an act which if done by a male person 16 years of age or over, or a female person 18 years of age or over, would make him or her liable to be arrested and prosecuted for the commission of a felony; or who has been adjudged a miscreant child under the Juvenile Code three or more times.

Miscreant is a boy less than 16 years of age, or a girl less than 18 years of age (other than a "traffic offender") who does an act which if done by a male person 16 years of age or over, or a female person 18 years of age or over, would make him or her liable to be arrested and prosecuted for the commission of a misdemeanor, or violation of ordinance, police regulation, or political subdivision order, rule or regulation; or who has been adjudged a wayward child under this act three or more times. (Wayward child is defined as a boy less than 16 years of age, or a girl less than 18 years of age whose behavior is injurious to his or her welfare; who has deserted his or her home without good or sufficient cause; who is habitually disobedient to the reasonable and lawful commands of parents, guardian or other lawful custodian.)

The *Boys' Industrial School,* with an emergency capacity of 190, receives delinquent and/or miscreant boys, as defined by the Juvenile Code, who are less than 16 years of age, who are committed by judges of county juvenile courts. The length of time a boy shall remain at the school is indefinite; the law provides that he shall remain until he is 21 years of age, unless sooner discharged.

Although there is nothing in the laws concerning a minimum age for commitment, the facilities of the institution make it undesirable to commit boys under the age of nine.

Boys are committed to the Boys' Industrial School by the Juvenile Courts to give them a chance to receive the particular help they need in solving their problems. To help the boy, it is necessary to understand him and the forces that have caused his problems. After arrival, each boy receives a physical, psychiatric, and dental examination, psychological and educational tests, and has a series of interviews with his caseworker. A program to meet the needs of the individual boy is then outlined including cottage life, medical care, education, vocational training, recreation, religion, social service, psychiatric service, psychological service, and other aspects of his institutional life.

When the institutional staff agrees that the boy has made satisfactory progress, and with a minimum of help should be able to deal adequately with his own problems outside the institution, he is recommended for parole. When he has successfully completed his parole period, he is recommended for discharge. The

(Continued on page 427)

The Kansas Press Looks at Medicine

Editor's Note. In this section the JOURNAL reproduces editorials relating to medicine which have appeared in the lay press. An effort is made to include both favorable and unfavorable comments, and the Editorial Board in no instance assumes responsibility for the opinions expressed.

PROOF OF THE PUDDING

There was a bit of irony in the news last week; quite a bit, in fact.

First came an announcement that Kansas has not had a single polio case reported since last September. A State Board of Health spokesman said this was the longest period the state has ever had without a polio case.

The next day, papers carried a story about Dr. Jonas E. Salk, who developed the vaccine responsible for Kansas' remarkable record this year. The great doctor was defending his vaccine against an attack by the American Medical Association. The association on June 28 had called for mass vaccination with a different "live" vaccine when it becomes available, and further asked that all persons who had already received Salk shots be given the new shots, too.

Dr. Salk, at a news conference, said he did not want to build any competition between the vaccines, but he saw no reason for revaccinating everybody with the new vaccine (developed by Dr. Albert Sabin). He suggested that his own vaccine had set up a new principle that could eventually lead to a single vaccine that would grant immunity to nearly 100 diseases.

The A.M.A. action, he indicated was based on an "old medical dogma" that says live vaccines are better than dead ones.

The man on the street certainly is in no position to take sides in this argument because of his lack of knowledge of science and medicine, and ignorance of clinical research. Doctors seem to pride themselves on using Latin or medical doubletalk that is impossible for laymen to understand, and this probably is just as well.

But most Americans are able to understand simple statistics. When a state that was once plagued each summer with hundreds of polio cases—many of them fatal—all of a sudden has no cases in 10 months, even the most ignorant can understand.

Dr. Jonas Salk developed a vaccine that has virtually wiped out one of this state's most dread diseases. The A.M.A. may not think his method is effective, but it will have a hard time convincing the residents in the Sunflower State.—R. C., *Emporia Gazette,* July 17, 1961.

MEDICAL PLAN FOR AGED

The fight to bring this nation a form of socialized medicine by providing medical aid for the aged through social security has flaws as well as good points. A proponent of the plan said it was all right for old people as long as it didn't interfere with the personal service his doctor gave him.

It's a little difficult to determine how the proposed medical program would affect the routine of the medical man. He might be obliged to treat all patients like a flock of sheep. Give them a shot as they walk by and quit when the clock strikes 5, leaving part of the flock waiting until next morning.

Americans have asked too much from their doctors for two reasons. They've bought health insurance and they have found that new drugs are quick to relieve illnesses which could be cured in a few days. Too many people with a cold refuse to smear on the goose grease and wait it out. Instead they rush up to the doctor and get a shot of smackus virus.

When it appears the illness will be drawn out the patient is placed in the hospital. Insurance pays the bill and of course, this is one way to collect a medical bill. It's surprising how many people don't pay the doctor for services. They change doctors instead.

From the financial standpoint, it doesn't seem right to put the medical program under social security.

Social security costs have been going up at regular intervals. Government doesn't ask the worker if he wants to contribute more. The money is extracted like income taxes. This is a place where the line could be held. Furthermore, it isn't wise to be tampering with the social security fund. It was meant for one purpose.

If this country needs a medical plan is should be set up as a separate program. It won't be many years until retired people can afford to carry on health insurance they had during their productive years. Insurance companies are moving in that direction. The people could sponsor their own medical plan if government would give them a chance.—*Arkansas City Daily Traveler,* July 14, 1961.

Need of Drug Control

The American Medical Association, predictably, has announced its opposition to a Senate bill slapping controls on the manufacture and distribution of medical drugs. Sen. Estes Kefauver, sponsor of the bill, says its principal aim is to "secure relief from a monopolistic industry" by cutting "generally unreasonable and excessive" drug prices.

An A.M.A. spokesman contended that most of the remedies in the bill should be left to the voluntary action of the A.M.A., the drug industry, and individual doctors.

Most people will agree that, ideally, voluntary reform would be preferable to government regulation; but the record encourages little hope of effective voluntary action. Last year's Senate hearings on the drug industry indicated that fondness for profits in some segments of the industry has outweighed regard for the bill-paying public. Even a trusting nature hesitates at believing that violators will voluntarily reduce profits and correct abuses; and the A.M.A.'s suggestion of voluntary reform implies an admission that such abuses do exist.

The proposed federal law, if reasonably drawn, will not damage the responsible part of the industry, any more than a speed limit damages a law-abiding driver. But the record, as brought out by the Kefauver investigation, plainly shows that such a law is needed. —*Wichita Eagle,* July 7, 1961.

Announcements

(Continued from page 420)

All physicians who are members of their county medical societies are cordially invited to attend. The complete program may be obtained by writing the Kansas City Southwest Clinical Society, 3036 Gillham Road, Kansas City 8, Missouri.

Blue Shield

(Continued from page 421)

information on National Accounts has not been furnished since each group usually has a unique set of benefits. However, such information is available from the local enrollment representative or through the Topeka Office of Blue Shield. Also, a reference chart is being prepared which should help in the interpretation of Blue Shield benefits.

From the Stacks

(Continued from page 422)

Mayo Clinic. Mayo clinic diet manual. Saunders. 1961.

Obstetrics & Gynecology

Greenhill, J. P. Obstetrics. Saunders. 1960.

Occupational Therapy

Dunton, W. R. Occupational therapy. C. C Thomas. 1960.

Book Reviews

(Continued from page 423)

ly emphasizes that the clinical diagnosis of an arrhythmia without the benefit of an electrocardiogram is usually unreliable. Hence this section is rather short. Part five consists of fifty-two electrocardiograms with which the reader can try his skill at diagnosing the various arrhythmias. The correct answers are given in the back of the volume.

This book is a valuable book for teaching the diagnosis and treatment of the various cardiac arrhythmias. It would be a useful reference for the doctor's office and the hospital emergency room.—*W.G.C.*

NEW MEMBERS

The Journal takes this opportunity to welcome these new members into the Kansas Medical Society.

Gene O. Harpster, M.D.
5832 Reeds Rd.
Mission, Kansas

Walter L. Reazin, M.D.
505 N. Hillside
Wichita 14, Kansas

Frank A. Mantz, M.D.
2912 West 73rd
Prairie Village, Kansas

Joseph H. Rohr, M.D.
5808 Nall Avenue
Mission, Kansas

John L. Nieman, M.D.
7501 Mission Road
Prairie Village, Kansas

Allen T. Stewart, M.D.
Valley Falls, Kansas

Personalities—IN KANSAS MEDICINE

Dr. Donald Marchbanks is closing his medical practice in Hill City and plans to open his office in Salina.

Dr. David Gray, Topeka, was elected president of the Science Fair board of directors.

Dr. B. L. Gardner, Winfield, is taking a leave of absence from his active practice of medicine in the near future to take postgraduate medical study at St. Mary's Hospital in Kansas City, Kansas. Upon completion of the work he will resume active practice in association with **Dr. J. H. Depoe,** Dr. C. D. Litton, and Dr. S. S. Daehnke.

Dr. Carl E. Olson has reopened his office in Fowler. The office has been closed for the past year as Dr. Olson has been taking advanced study in medicine at the University of Kansas Medical Center.

Dr. Lafe Bauer closed his active practice in Smith Center to move his family to Shawnee Mission, Kansas.

Dr. E. N. Robertson, Concordia, attend the American Medical Association convention in New York.

Dr. Frank L. Menehan, a founder of the Wichita Medical Clinic, recently announced his retirement. A pediatrician in Wichita since 1932, he founded and practiced at the clinic since 1948. Dr. and Mrs. Menehan will move to La Jolla, California.

The American College of Chest Physicians held its 27th Annual Meeting in New York City, June 22-26. At the convocation on June 25, fellowship certificates were conferred on 204 physicians. Recipients of these certificates from Kansas are **E. Ernest Johnson, Jr., M.D.,** Norton and B. G. Achar, M.D., Wadsworth.

Editorial Comment

(Continued from page 424)

discharge certificate is signed by the institution superintendent.

For certain offenses, such as repeated escapes, destruction of state property, or assault upon employees, the institution may petition the district court to sentence a boy to the State Industrial Reformatory at Hutchinson.

The *Girls' Industrial School,* with a capacity of 90, receives delinquent and/or miscreant girls, as defined by the Juvenile Code, who are less than 18 years of age, who are committed by judges of county juvenile courts. No legal minimum age for commitment is provided, however, the program of care, treatment, and training is best fitted for teen-age girls, with emphasis on education, vocational training and home living.

Psychiatric services, psychological and social service counseling, religious instruction, academic and commercial education and vocational training, recreational activities and the department of homelife and cottage program are utilized in the school's activities. The treatment and training program is adapted to the individual needs of the girl in an effort to return her as soon as possible to her family and community.

A committed girl remains until 21 years of age, unless sooner discharged. The discharge is issued by the superintendent of the institution and usually follows a parole period. For certain offenses such as repeated escapes, destruction of state property, or assault upon employees, the institution may petition the district court to sentence the girl to the Women's Industrial Farm at Lansing.

KMS Obituaries

ALPHA D. UPDEGRAFF, M.D.

Dr. A. D. Updegraff, 83, Wichita physician and surgeon until his retirement two years ago, died July 28 at his home in Valley Center.

Born June 12, 1878, at Pretty Prairie, Kansas, Dr. Updegraff began his practice in 1901 at Kansas City, Kansas, following his graduation from the College of Physicians and Surgeons in Kansas City. In 1902, he moved to Anthony, Kansas, where he continued his practice until moving to Wichita in 1912.

He is survived by his wife, Edna, and one son, Alpha M., of Valley Center; two grandchildren and four great-grandchildren.

GEORGE A. WESTFALL, JR., M.D.

Dr. G. A. Westfall, Jr., 42, Halstead, Kansas, died at the Halstead Hospital on July 22 of hemochromatosis and portal cirrhosis with massive esophageal hemorrhage.

He was born February 8, 1919, in Harper, Kansas. He graduated from the University of Kansas in 1944 with his M.D. degree. He joined the staff of the Hertzler Clinic and the Halstead Hospital in 1949 and served as Hematologist in the Department of Internal Medicine until his death.

Surviving him are his widow, Edna Lucile and two children, Marcia Ann 12, and George, III, 10. Also by his mother, Della Westfall and one brother, Dr. Cad Westfall of Fort Worth, Texas.

GROVER G. WHITLEY, M.D.

Dr. Grover G. Whitley, 68, long-time physician in Douglass, died July 10 in Winfield. He retired from active practice in 1955.

Born August 29, 1892, he was graduated from Tulane University, New Orleans, in 1916. He moved to Douglass in 1919 following service with the medical corps in World War I. He went into practice with Dr. Arthur W. Fegtly, now of Wichita, for quite a number of years.

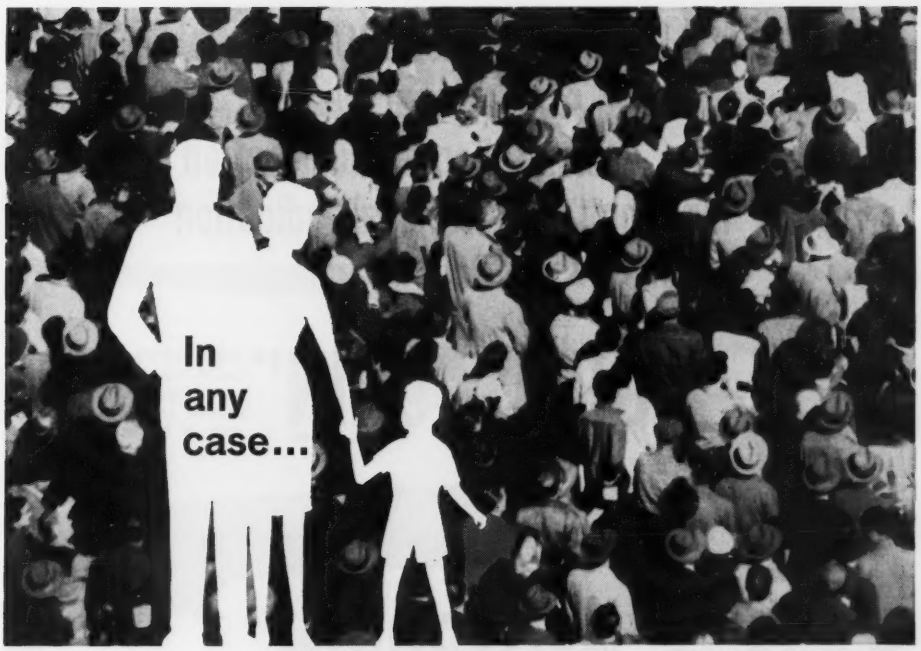
He is survived by his wife, Florence, a daughter, three grandchildren and a sister.

ERNEST D. WILLIAMS, M.D.

Dr. E. D. Williams, 90, Kansas City, long-time physician and surgeon and former county coroner, died in his home on July 8 after a two year illness.

Born in Manhattan, Kansas, August 28, 1870, he graduated from the University Medical College of Kansas City in 1899 and began practicing medicine in Armourdale. He retired from active practice in 1952. In 1911 he founded the Lifelone Orphanage which is now known as the Lifelone Children's Home.

Surviving are his wife, Mrs. Beryl M. Williams, of the home, a daughter of California; two granddaughters and five great-granddaughters.



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Such striking antidiarrheal activity strongly suggests that Lomotil is the drug of *first* choice for prompt and positive control of diarrhea.

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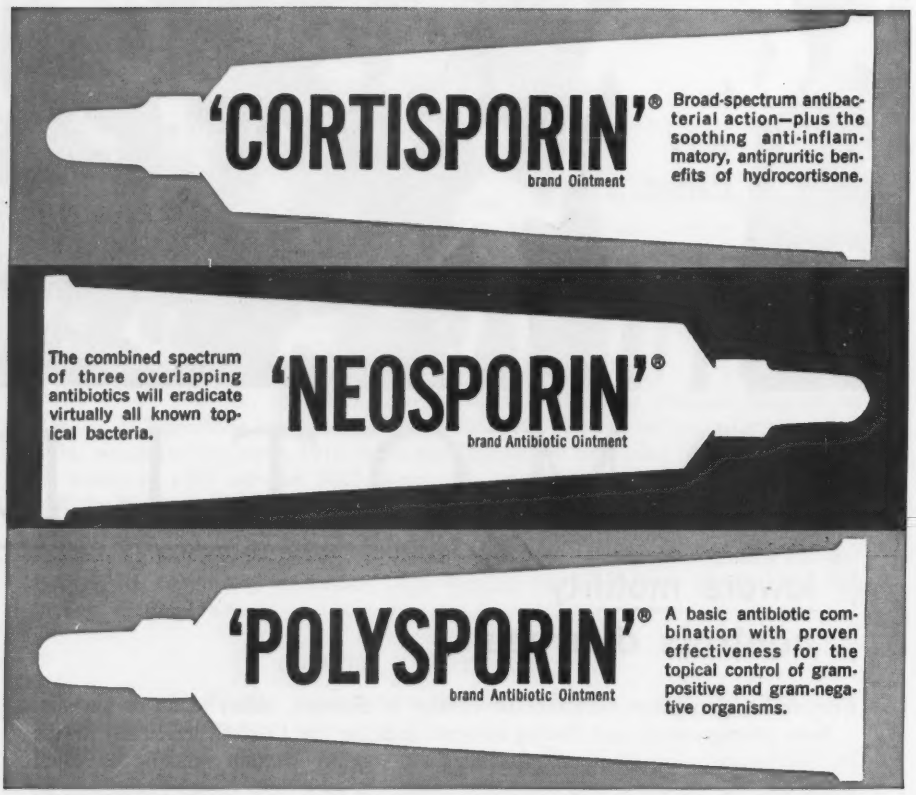
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Contents per Gm.	'Polysporin'®	'Neosporin'®	'Cortisporin'®
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Zinc Bacitracin	500 Units	400 Units	400 Units
Neomycin Sulfate	—	5 mg.	5 mg.
Hydrocortisone	—	—	10 mg.
Supplied:	Tubes of 1 oz., ½ oz. and ⅛ oz. (with ophthalmic tip)	Tubes of 1 oz., ½ oz. and ⅛ oz. (with ophthalmic tip)	Tubes of ½ oz. and ⅛ oz. (with ophthalmic tip)

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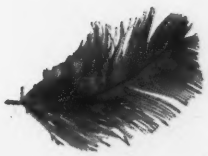

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References: 1. Santos, I. M. H., and Unger, L.: Ann. Allergy 18:172 (Feb.) 1960. 2. Charlton, J. D.: Ann. Allergy, in press. 3. Shaftel, H. E.: Clin. Med. 7:1841 (Sept.) 1960.

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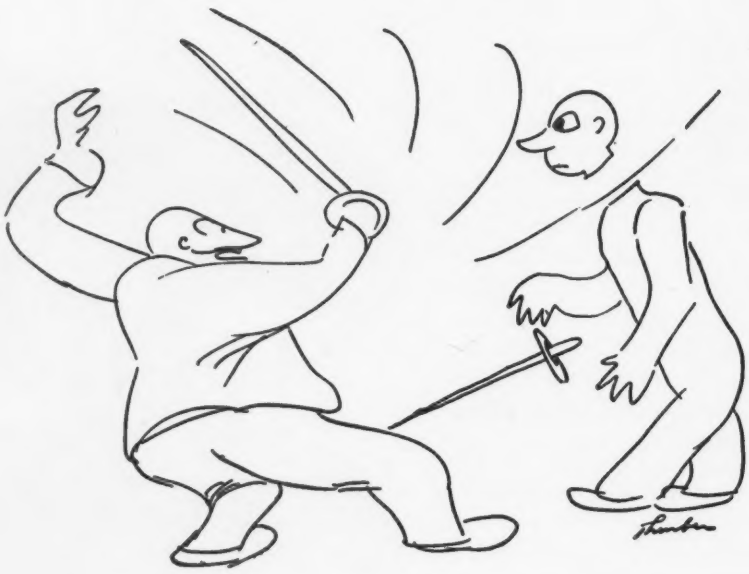

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How Trancoprin relieves pain: Because most pain is accompanied by muscle spasm and tension, good medical practice suggests use of an analgesic that will relax skeletal muscles as well as dim pain perception. Such an analgesic is Trancoprin — a combination of aspirin and Trancopal®, a proved, safe, skeletal muscle relaxant and tranquilizer. Trancoprin can be prescribed for any pain, except pain of such severity that a narcotic is needed.

Dosage: Adults, 2 tablets three or four times daily; children (5 to 12 years), 1 tablet three or four times daily. Each tablet contains 300 mg. of aspirin and 50 mg. of Trancopal (brand of chlormezanone). Bottles of 100 tablets.

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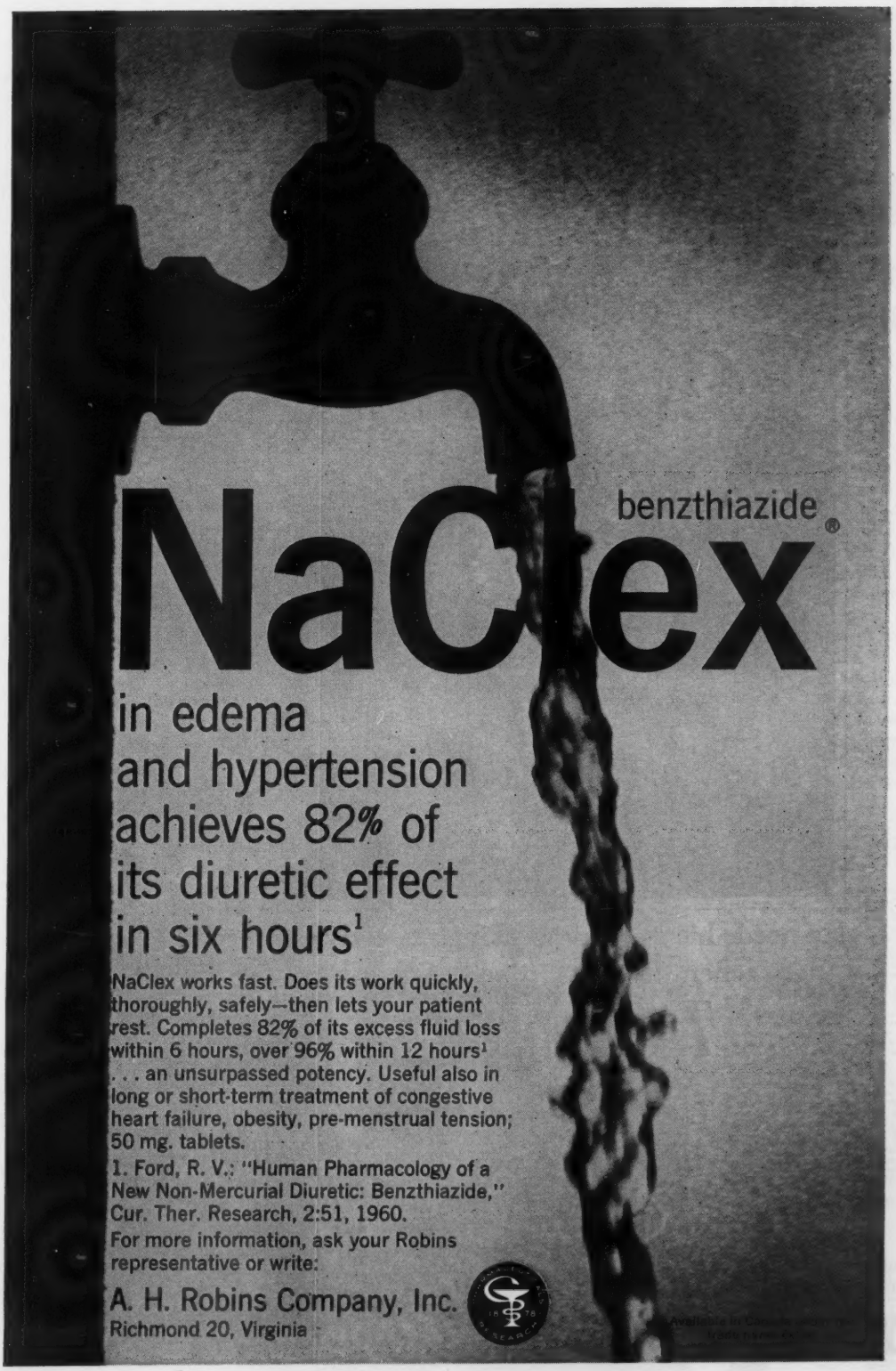
benzthiazide®
NaClex
in edema
and hypertension
achieves 82% of
its diuretic effect
in six hours[1]
NaClex works fast. Does its work quickly, thoroughly, safely—then lets your patient rest. Completes 82% of its excess fluid loss within 6 hours, over 96% within 12 hours[1] . . . an unsurpassed potency. Useful also in long or short-term treatment of congestive heart failure, obesity, pre-menstrual tension; 50 mg. tablets.
1. Ford, R. V.: "Human Pharmacology of a New Non-Mercurial Diuretic: Benzthiazide," Cur. Ther. Research, 2:51, 1960.
For more information, ask your Robins representative or write:
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He needs his muscles working properly—
when they aren't, he needs
Trancopal

How to use *Trancopal*®
Brand of chlormezanone
for painful muscles

When a muscle is strained, it goes into a spasm that produces pain; this is followed by more spasm for splinting, and then more pain.

When you prescribe Trancopal, you break this vicious cycle and relieve the patient's discomfort. Trancopal will ease the spasm and consequently the pain, and its mild tranquilizing effect will make the patient less restless. You can then start him on purposeful exercise or physical therapy.

In addition to its usefulness in syndromes resulting from overstraining (such as low back pain or tennis elbow), Trancopal will relax the spasm and pain that are features of torticollis, bursitis, fibrositis, myositis, ankle sprain, osteoarthritis, rheumatoid arthritis, disc syndrome and postoperative muscle spasm. Trancopal is available in 200 mg. Caplets® (green colored, scored) and in 100 mg. Caplets (peach colored, scored), bottles of 100.

Dosage: Adults, 1 Caplet (200 mg.) three or four times daily; children (5 to 12 years), from 50 to 100 mg. three or four times daily.

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1626M

in bacterial otitis media

Panalba* promptly

to gain precious therapeutic hours

In the presence of bacterial infection, taking a culture to determine bacterial identity and sensitivity is desirable—but not always practical.

A rational clinical alternative is to launch therapy at once with Panalba, the antibiotic that provides the best odds for success.

Panalba is effective (in vitro) against 30 common pathogens, including the ubiquitous staph. Use of Panalba *from the outset* (even pending laboratory results) can gain precious hours of effective antibiotic treatment.

SUPPLIED: Capsules, each containing Panmycin* Phosphate (tetracycline phosphate complex), equivalent to 250 mg. tetracycline hydrochloride, and 125 mg. Albamycin,* as novobiocin sodium, in bottles of 16 and 100.

USUAL ADULT DOSAGE: 1 or 2 capsules 3 or 4 times a day.

SIDE EFFECTS: Panmycin Phosphate has a very low order of toxicity comparable to that of the other tetracyclines and is well tolerated clinically. Side reactions to therapeutic use are infrequent and consist principally of mild nausea and abdominal cramps.
Albamycin also has a relatively low order of toxicity. In a certain few patients, a yellow pigment has been found in the plasma. This pigment, apparently a metabolic by-product of the drug, is not necessarily associated with abnormal liver function tests or liver enlargement.
Urticaria and maculopapular dermatitis, a few cases of leukopenia and agranulocytosis have been reported in patients treated with Albamycin. These side effects usually disappear upon discontinuance of the drug.

CAUTION: Since the use of any antibiotic may result in overgrowth of nonsusceptible organisms, constant observation of the patient is essential. If new infections appear during therapy, appropriate measures should be taken. Total and differential blood counts should be made routinely during prolonged administration of Albamycin. The possibility of liver damage should be considered if a yellow pigment, a metabolic by-product of Albamycin, appears in the plasma. Panalba should be discontinued if allergic reactions that are not readily controlled by antihistaminic agents develop.

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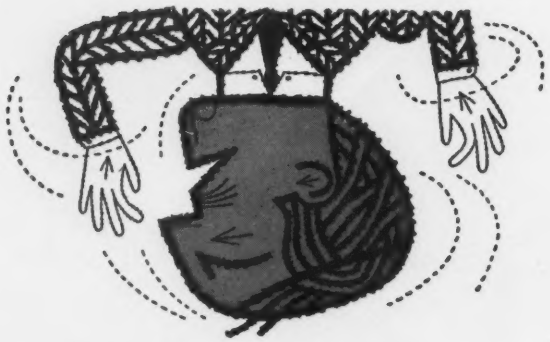

vertigo is reversible

Antivert® stops vertigo

moderate to complete relief of symptoms in 9 out of 10 patients[1]

Prescribe one ANTIVERT tablet (or 1-2 teaspoonfuls ANTIVERT syrup) 3 times daily, before each meal, for prompt relief of vertigo, Meniere's syndrome and allied disorders. Side effects are short-lived, usually only harmless flushing and tingling associated with vasodilation. As with all vasodilators, ANTIVERT is contraindicated in severe hypotension and hemorrhage.

Supplied: Small blue-and-white scored tablets (meclizine HCl 12.5 mg. and nicotinic acid 50 mg.) in bottles of 100. Syrup (each 5 cc. teaspoonful contains meclizine HCl 6.25 mg. and nicotinic acid 25 mg.) in pint bottles. Prescription only. Bibliography available on request.

Reference: 1. Scal, J. C.: Eye Ear Nose & Throat Month. 38:738 (Sept.) 1959.

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YOUR RESULTS: With pain relieved, stiffness gone, your patient is soon restored to full activity—often in days instead of weeks.

Kestler reports in controlled study: *Average time for restoring patients to full activity: with Soma, 11.5 days; without Soma, 41 days.* (*J.A.M.A. Vol. 172, No. 18, April 30, 1960.*)

Soma is notably safe. Side effects are rare. Drowsiness may occur, but usually only in higher dosages. Soma is available in 350 mg. tablets. **USUAL DOSAGE: 1 TABLET Q.I.D.**

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(carisoprodol, Wallace)

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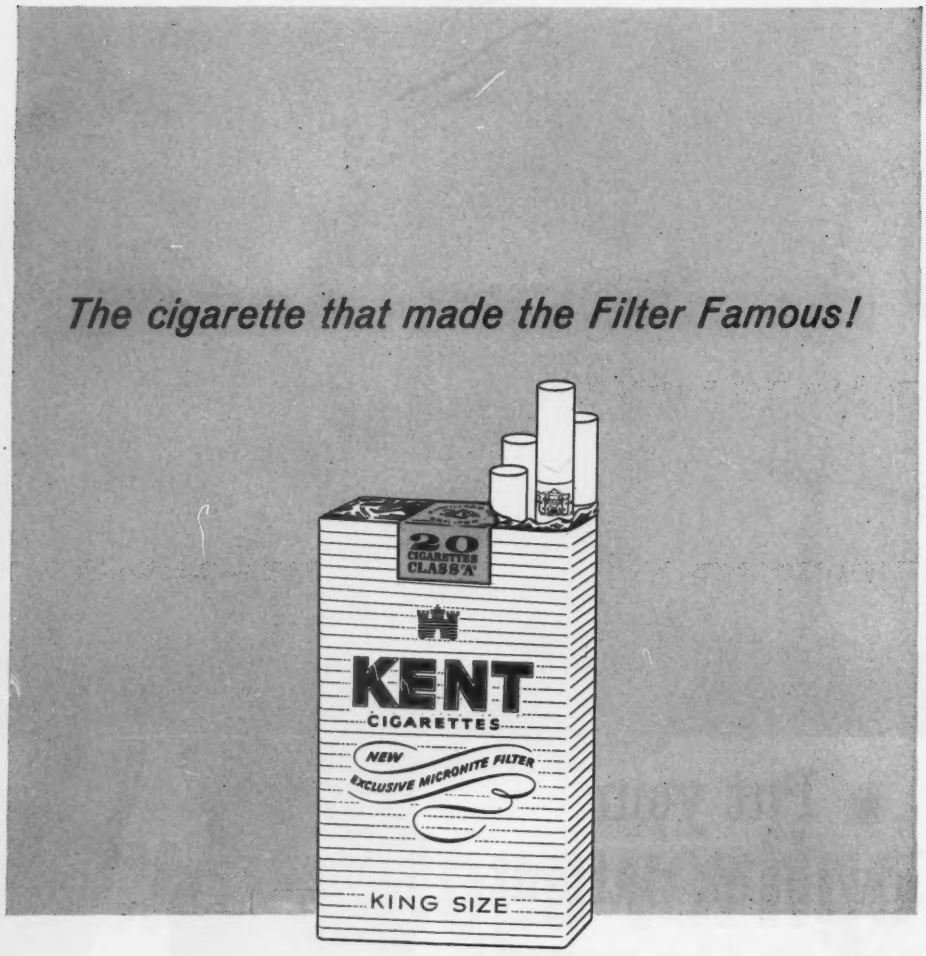

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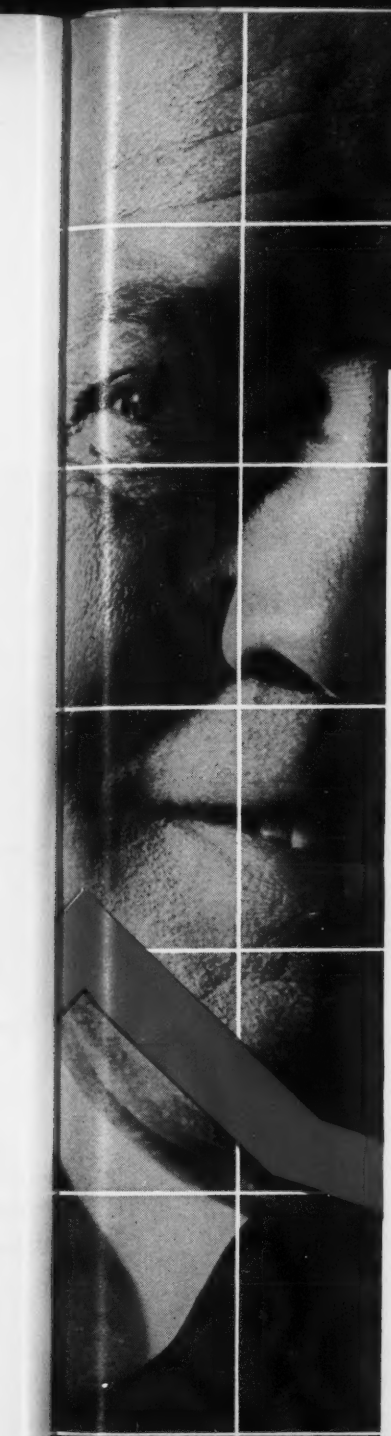

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CLINICAL & PHARMACOLOGICAL REPORTS 1. Berger, F. M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W-583). Fed. Proc. *20*:113 (March) 1961. 2. Diamond, S., and Schwartz, M. Scientific Exhibit at Ill. State Med. Soc. Chicago, (May) 1961. 3. Douglas, J. F. Ludwig, B. J., Ginsberg, T. and Berger, F. M.: Studies on W-583 Metabolism. Fed. Proc. *20*:113 (March) 1961. 4. Duarte, C., Brest, A. N., Kodama, R., Naso, F., and Moyer, J. H.: Observations on the Antihypertensive Effectiveness of a New Propanediol Dicarbamate (W-583). Curr. Ther. Res., *2*:148-52 (May) 1960. 5. DuChez, J. W., Scientific Exhibit at Amer. Academy of Gen. Practice, Miami, (April) 1961. 6. Kletzkin, M., and Berger, F. M.: A Centrally Acting Antipressor Agent. Fed. Prod. *20*:113 (March) 1961. 7. Mulinos, M. G., Scientific Exhibit at Amer. Coll. Card. New York, (May) 1961. 8. Mulinos, M. G., Saltefors, S., Boyd, L. J. and Cronk, G. A.: Human Pharmacology Studies with W-583. Fed. Proc. *20*:113 (March) 1961. 9. Shubin, H., Scientific Exhibit, Amer. Coll. Card. New York, (May) 1961.

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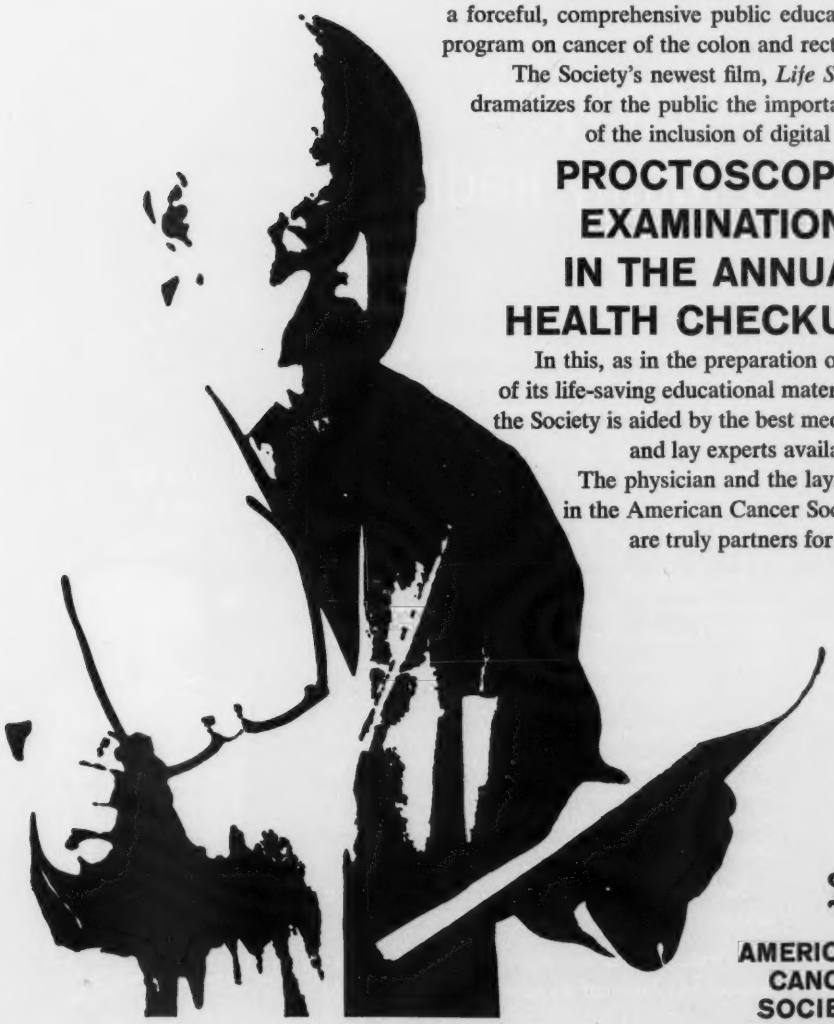

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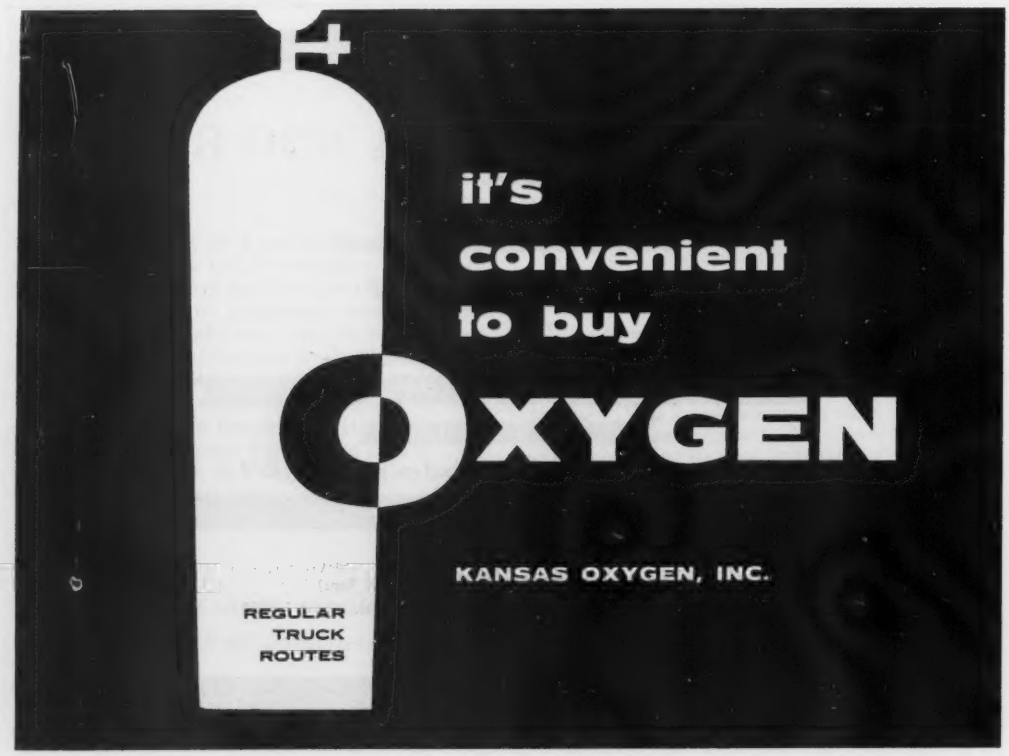

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(1) Danowski, T. S.: Diabetes Mellitus, Baltimore, Williams & Wilkins, 1957, p. 239. (2) McCune, W. G.: M. Clin. North America 44:1479, 1960. (3) Ackerman, R. F., et al.: Diabetes 7:398, 1958.

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